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Inside this issue: Measles in Canada

In 2002 the Americas gained elimination status for measles, yet over 10 years later we continue to have imported cases and limited outbreaks. Read this issue to find out what's happened with measles in Canada, why we haven't lost our elimination status despite the outbreaks, why we *have* outbreaks and how we have dealt with them, the detective role that genotyping plays, and what it will take to maintain our elimination status.

Surveillance

Measles surveillance in Canada: Trends for 2013 219
Shane A, Hiebert J, Sherrard L and Deehan H

Rapid communication

Measles activity in Canada: January – June 2014 233
Deehan H and Shane A

Surveillance and outbreak reports

Measles-containing vaccination rates in southern Alberta 236
Matkin A, Simmonds K and Suttorp V

Outbreak of measles in a non-immunizing population, Alberta 2013 243
Kershaw T, Suttorp V, Simmonds K and St. Jean T

A community outbreak of travel-acquired measles, Ontario 2009 251
Armstrong J, Arajs A, Bailey N and Wang HL

Overview

Measles molecular epidemiology: What does it tell us and why is it important? 257
Hiebert J and Severini A

Invited editorial

The challenges of sustaining measles elimination in Canada 261
Crowcroft NS

Useful links

Guidelines for the prevention and control of measles outbreaks in Canada. Measles and Rubella Elimination Working Group. CCDR 2013:39: ACS-3.

http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-3/assets/pdf/meas-roug-eng.pdf

***Clinical Update*: A comparison of adult and pediatric measles patients admitted to emergency departments during the 2008-2011 outbreak in the Midi-Pyrénées region of France.**

Casasoprana A, Honorat R, Grouteau E, Marchou B, Claudet I. Jpn J Infect Dis. 2014;67(2):71-7.

http://www.ncbi.nlm.nih.gov/pubmed/24647247

Public Health Agency of Canada: Measles webpage

Next Issue July 10th, 2014: Hepatitis B

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Canada

Measles surveillance in Canada: Trends for 2013

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ABSTRACT

Objective: The objective of this report is to describe measles activity in Canada during 2013, in order to support the documentation and maintenance of measles elimination status.

Methods: A descriptive analysis of measles counts and incidence by age group, immunization history, hospitalization and province/territory, as well as a summary of 2013 outbreaks, was conducted using enhanced measles data captured through the Canadian Measles and Rubella Surveillance System. Genotype information and phylogenetic analysis for 2013 were summarized.

Results: In 2013, 83 confirmed measles cases were reported in seven provinces/territories for an incidence rate of 2.4 per 1,000,000 population. Incidence was highest in the youngest age groups (< 1 year, 1 to 4 years). Burden of disease was highest in the youngest age groups and children 10 to 14 years. Three-quarters of cases had been inadequately immunized, and 10% were hospitalized. There were nine measles outbreaks reported in 2013, one of which consisted of 42 cases in a non-immunizing community in Alberta.

Discussion: 2013 saw the fifth highest number of reported measles cases since 1998. While we continue to face challenges related to importation and heterogeneous immunization coverage, in 2013 Canada met or partially met all four criteria outlined by the Pan American Health Organization for measles elimination.

Introduction

The last reported case of endemic measles in Canada occurred in November 1997; Canada's elimination status was achieved one year later in 1998 (1). The World Health Organization (WHO) Region of the Americas achieved elimination status in 2002, making it the first and only WHO Region to reach this goal. Elimination of measles is maintained as long as a single measles viral strain is not circulating continuously throughout Canada for a period of 12 months or more (2). Endemic measles activity persists across the European, African, Southeast Asian and Western Pacific regions (3). While endemic transmission has not been re-established in Canada, the possibility of importation of measles into the country remains, as a result of population exchange with endemic countries or countries experiencing measles outbreaks.

Subsequent outbreaks within Canada following a measles importation are often limited; however, there were large outbreaks of 94, 53, 82 and 678 cases in 2007, 2008, 2010 and 2011 (4, 5). Transmission within Canada is associated with those who are under- or unimmunized and areas with suboptimal immunization coverage. While 2-dose immunization coverage in Canada is generally high (the 2011-12 Childhood National Immunization Survey estimated 2-dose coverage by age 7 years to be 94.9% [6]), it is not uniform across the country, within provinces and territories, or across sub-populations (e.g. religious communities that oppose vaccination). Given the lack of uniformity in coverage to achieve the ≥ 95% coverage recommended for measles herd immunity (7), the risk of domestic transmission following an importation of measles remains a reality.

As an ongoing component of Canada's commitment to the maintenance and documentation of measles elimination status, the Public Health Agency of Canada (the Agency) conducts enhanced measles surveillance. The post-elimination Canadian measles epidemiology has been previously reported for 1998-2001 (1) and 2002 to 2011 (4). There were only 10 confirmed measles cases reported in Canada in 2012, the majority (n = 6, 60.0%) of them importations without secondary spread. Information on these cases is available elsewhere (8). The

objective of this report, therefore, is to describe measles activity in Canada during 2013, in order to support the documentation and maintenance of measles elimination status.

Methods

Surveillance dataset

Enhanced measles surveillance is carried out in all provinces and territories through the Canadian Measles and Rubella Surveillance System. On a weekly reporting cycle, provinces and territories report cases of measles meeting the national case definition (9) to the Agency, including zero reporting, through a national case report form that is submitted by e-mail or fax. Three jurisdictions (British Columbia, Alberta, and Newfoundland and Labrador) are currently participating in the Measles and Rubella Surveillance pilot project, which provides real-time laboratory and epidemiological web-based reporting of suspect measles/rubella case investigations. Case details obtained from the national surveillance system case report forms and Measles and Rubella Surveillance web-based notifications were assessed against the national measles confirmed-case definition (laboratory confirmed or epidemiological link to a laboratory-confirmed case) before inclusion in the national database.

The objective of national measles surveillance is to continuously monitor the presence of measles virus in Canada in a timely way. To meet this objective, the Canadian Measles and Rubella Surveillance System captures cases that were communicable in Canada, regardless of country of residence. This allows accurate international and national reporting of the presence of measles virus in Canada, which is an essential criterion for measles elimination. However, this might result in case count discrepancies between federal and provincial/territorial surveillance systems, since some provincial/territorial systems do not include measles cases among foreign nationals.

This report includes enhanced data of confirmed measles cases, reported by the provinces and territories through both the national surveillance system and the surveillance pilot project, with rash onset during epidemiological weeks 1 to 52 for the 2013 reporting year (i.e. from December 30, 2012, to December 28, 2013). Probable cases (9) are not nationally notifiable and therefore are not included in this report.

Case report form

The Canadian Measles and Rubella Surveillance System case report form is one page in length and designed to meet the objectives of national surveillance. The form facilitates collection of information on case identifiers (date of birth or age, gender, health unit, city, forward sortation area, date reported to health unit and date investigation was started); background, exposure and clinical information (date of rash onset, hospitalization, source of exposure, vaccination history [date of each dose] and whether the case was outbreak associated); and laboratory information (results of laboratory tests).

The data manager followed up with the reporting jurisdiction if information was missing on the form. At data entry, values coded as missing represented those that were blank on the form, and values coded as unknown represented those sought, but not available, from the reporting jurisdiction. A data validation process was conducted with provinces and territories in March 2014 for all measles cases reported nationally in 2013.

Genotyping

Measles virus genotyping was performed at the Public Health Agency of Canada's National Microbiology Laboratory. Appropriate clinical specimens (respiratory specimens and/or urines) collected from suspect or confirmed measles cases were submitted by provincial laboratories. The WHO's standardized genotyping regions of the 450 nucleotides encoding the carboxyl-terminus of the measles nucleoprotein, the N-450, and the full length hemagglutinin gene (H gene) (10) were amplified and sequenced from extracted nucleic acid. The sequences were aligned with WHO genotype reference sequences (11), and phylogenetic trees were generated using MEGA5 software (12).

Data management and statistical analysis

Data management was conducted with Microsoft Access 2010. Descriptive epidemiological analyses were conducted with SAS Enterprise Guide 5.1 (13). Distribution of confirmed measles cases by province and territory, age group, sex, immunization history and hospitalization were described. Case counts and proportions were calculated for categorical variables, and means/medians and ranges were calculated for continuous variables. Cases with missing or unknown responses were included in the denominators for proportions. Incidence rates were generated using population estimates from Statistics Canada for 2013 (14). Rates were calculated per 1,000,000 population for consistency with the PAHO recommended indicator (2).

The National Advisory Committee on Immunization's recommendations for measles immunization was used to determine whether cases' immunization status was up to date for age with measles-containing vaccine (15). Children aged < 1 year and adults born before 1970 were considered up to date for age with 0 or more doses of measles-containing vaccine. Cases aged 1 to 6 years were considered up to date for age with one or more doses of measles-containing vaccine and those aged 7 years and older (but born in 1970 or later) were up to date with two or more doses.

Essential criteria for measles elimination

In order to continue documentation and verification of measles elimination in the Region of the Americas, the Pan-American Health Organization (PAHO) has developed four criteria that it considers essential for each Member State to meet (2):

1. Verify the interruption of endemic measles cases for a period of at least three years from the last known endemic case, in the presence of high-quality surveillance;
2. Implement and maintain high-quality surveillance sensitive enough to detect imported and import-related cases;
3. Verify the absence of endemic measles virus strains through viral surveillance; and
4. Verify adequate immunization in the population.

Canada's performance towards maintenance of measles elimination was assessed against the four elimination criteria on the basis of the 2013 Canadian surveillance data.

This study was exempt from research ethics board approval because the data set was the result of public health surveillance.

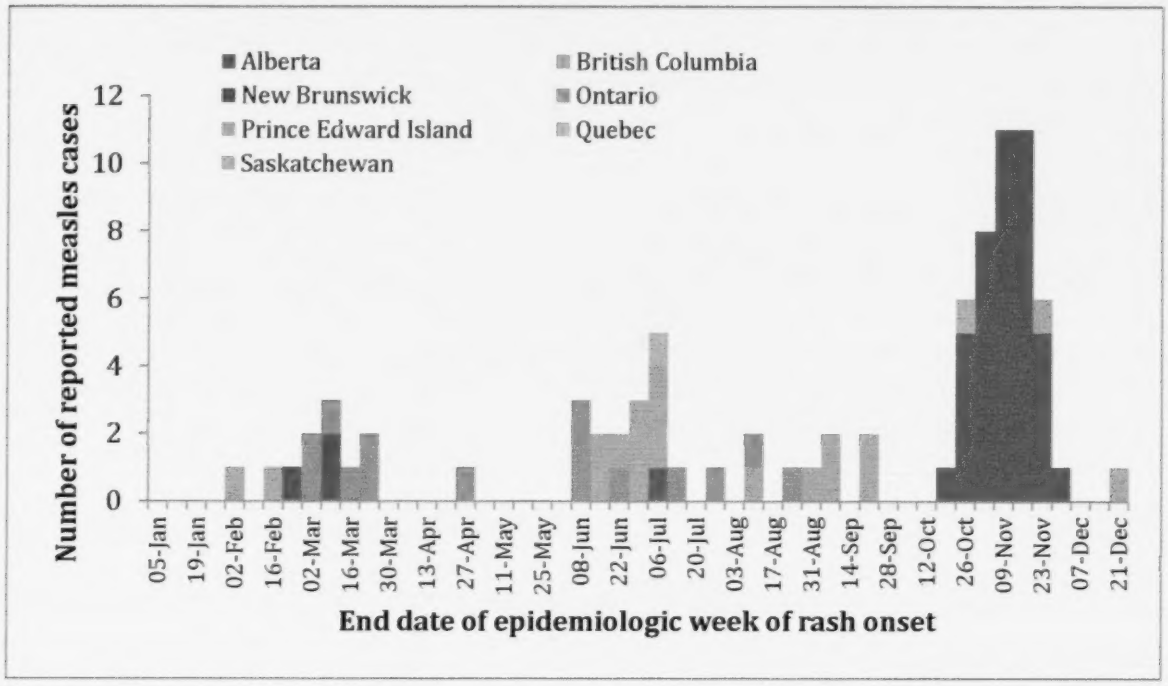
Results

Overview

In 2013, a total of 83 confirmed measles cases were reported, for an overall incidence rate of 2.4 cases per 1,000,000 population. Of these cases, 53 (63.9%) were laboratory confirmed and 30 (36.1%) were epidemiologically linked to a laboratory-confirmed case.

Measles cases were reported in seven provinces and territories over 28 weeks in 2013. The maximum number of cases that occurred per week was 11, in weeks 45 and 46. These were outbreak-associated cases that occurred during the peak of a large outbreak in Alberta (**Figure 1**).

Figure 1. Number of reported measles cases by epidemiological week of rash onset and reporting province or territory, Canada, 2013



Age, gender and geographic distribution

The majority of measles cases reported were male (n = 45, 54.2%). Children aged 1 to 4 years and 10 to 14 years each represented the highest proportion of cases (n = 17 and 20.5% each), followed by 15 to 19 and 20 to 24 year olds (n = 11 and 13.3% each). Of the four cases aged 40 years and older, three were born before 1970, the birth year cut-off for presumed natural immunity (15).

While the burden of disease extended from those aged 1 to 24 years, the incidence rate was highest among the youngest age groups (10.5 per 1,000,000 for those < 1 year; 11.0 per 1,000,000 for those 1 to 4 years) (**Table 1**).

Table 1. Confirmed measles cases and incidence rates (per 1,000,000 population) by age group, gender and reporting province or territory, Canada, 2013

Age group (years)	M	F	CA	BC	AB	SK	MB	ON	QC	NB	NS	PE	NL	YT	NT	NU	Overall incidence rate
< 1	4	0	4	2	1	0	0	1	0	0	0	0	0	0	0	0	10.5
1 to 4	12	5	17	1	6	0	0	7	1	2	0	0	0	0	0	0	11.0
5 to 9	6	3	9	0	7	0	0	2	0	0	0	0	0	0	0	0	4.8
10 to 14	6	11	17	1	15	0	0	0	0	0	0	1	0	0	0	0	9.1
15 to 19	5	6	11	0	9	0	0	1	0	0	0	1	0	0	0	0	5.0
20 to 24	4	7	11	5	5	1	0	0	0	0	0	0	0	0	0	0	4.5
25 to 29	2	2	4	3	0	0	0	1	0	0	0	0	0	0	0	0	1.7
30 to 39	6	0	6	3	0	0	0	2	0	1	0	0	0	0	0	0	1.3

Age group (years)	M	F	CA	BC	AB	SK	MB	ON	QC	NB	NS	PE	NL	YT	NT	NU	Overall incidence rate
40 to 59	0	4	4	2	0	0	0	2	0	0	0	0	0	0	0	0	0.4
≥60	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	**45**	**38**	**83**	**17**	**43**	**1**	**0**	16*	**1**	**3**	**0**	**2**	**0**	**0**	**0**	**0**	**2.4**
Incidence rate	2.6	2.1	2.4	3.7	10.7	0.9	0	1.2	0.1	4.0	0	13.8	0	0	0	0	2.6

M: male; F: female; CA: Canada

*One Ontario case was a traveller from the Netherlands and is not included in Ontario's provincial measles case counts of 15 for 2013.

Cases were reported in 7 of the 13 Canadian provinces and territories: Alberta (n = 43), British Columbia (n = 17), Ontario (n = 16), New Brunswick (n = 3), Prince Edward Island (n = 2), Quebec (n = 1) and Saskatchewan (n = 1). The incidence rate was highest in Prince Edward Island, given its small population, followed by Alberta, with 13.8 and 10.7 cases per 1,000,000 population respectively. The incidence for the each of the remaining provinces was less than 5.0 cases per 1,000,000 population (**Table 1**).

Immunization history

Of the 83 cases reported in 2013, 13.3% (n = 11) had an immunization status considered up to date for age (**Table 2**). These included four infants < 1 year who were too young to receive their first dose of measles-containing vaccine and one adult born before 1970. Conversely, 75.9% (n = 63) were not up to date for age at the time of infection and immunization status was unknown for 10.8% (n = 9); two of these were born before 1970 and are presumed to be immune regardless of immunization history.

Table2. Immunization status of confirmed measles cases by age group, Canada, 2013

Age group (years)	TOTAL	0 doses	*Up To Date with* 0 doses	One dose	*Up To Date with* 1 dose	Two doses	Unknown
< 1	4	4	4	0	-	0	0
1 to 4	17	14	0	2	2	1	0
5 to 9	9	9	0	0	-	0	0
10 to 14	17	17	0	0	-	0	0
15 to 19	11	10	0	0	-	1	0
20 to 24	11	7	0	0	-	2	2
25 to 29	4	3	0	1	0	0	0
30 to 39	6	1	0	0	-	0	5
40 to 59	4	2	1	0	-	0	2
≥60	0	0	-	0	-	0	0
Unknown	0	0	-	0	-	0	0
TOTAL	**83**	**67**	**5**	**3**	**2**	**4**	**9**

Mirroring the age group distribution of the cases, inadequate immunization status was most commonly reported in the 10 to 14 and 1 to 4 year age groups (27.0% and 22.2% respectively), followed by the 5 to 9 and 15 to 19 year olds (14.3 and 15.9% respectively).

Hospitalization

Of the 83 reported cases, 9.6% (n = 8) were hospitalized (**Table 3**). Half of the infants < 1 year and 30% of cases among adults 25 to 39 years were hospitalized. Hospitalization was infrequent among cases 1 to 24 years of age.

Table 3. Hospitalization status of confirmed measles cases by age group, Canada, 2013

Age group (years)	TOTAL	Not hospitalized, no. (%)	Hospitalized no. (%)	Unknown no. (%)
< 1	4	2 (50.0)	2 (50.0)	0 (-)
1 to 4	17	14 (82.4)	2 (11.8)	1 (5.9)
5 to 9	9	9 (100.0)	0 (-)	0 (-)
10 to 14	17	17 (100.0)	0 (-)	0 (-)
15 to 19	11	10 (90.9)	1 (9.1)	0 (-)
20 to 24	11	11 (100.0)	0 (-)	0 (-)
25 to 29	4	3 (75.0)	1 (25.0)	0 (-)
30 to 39	6	4 (66.7)	2 (33.3)	0 (-)
40 to 59	4	4 (100.0)	0 (-)	0 (-)
≥60	0	0 (-)	0 (-)	0 (-)
Unknown	0	0 (-)	0 (-)	0 (-)
TOTAL	**83**	**74 (89.2)**	**8 (9.6)**	**1 (1.2)**

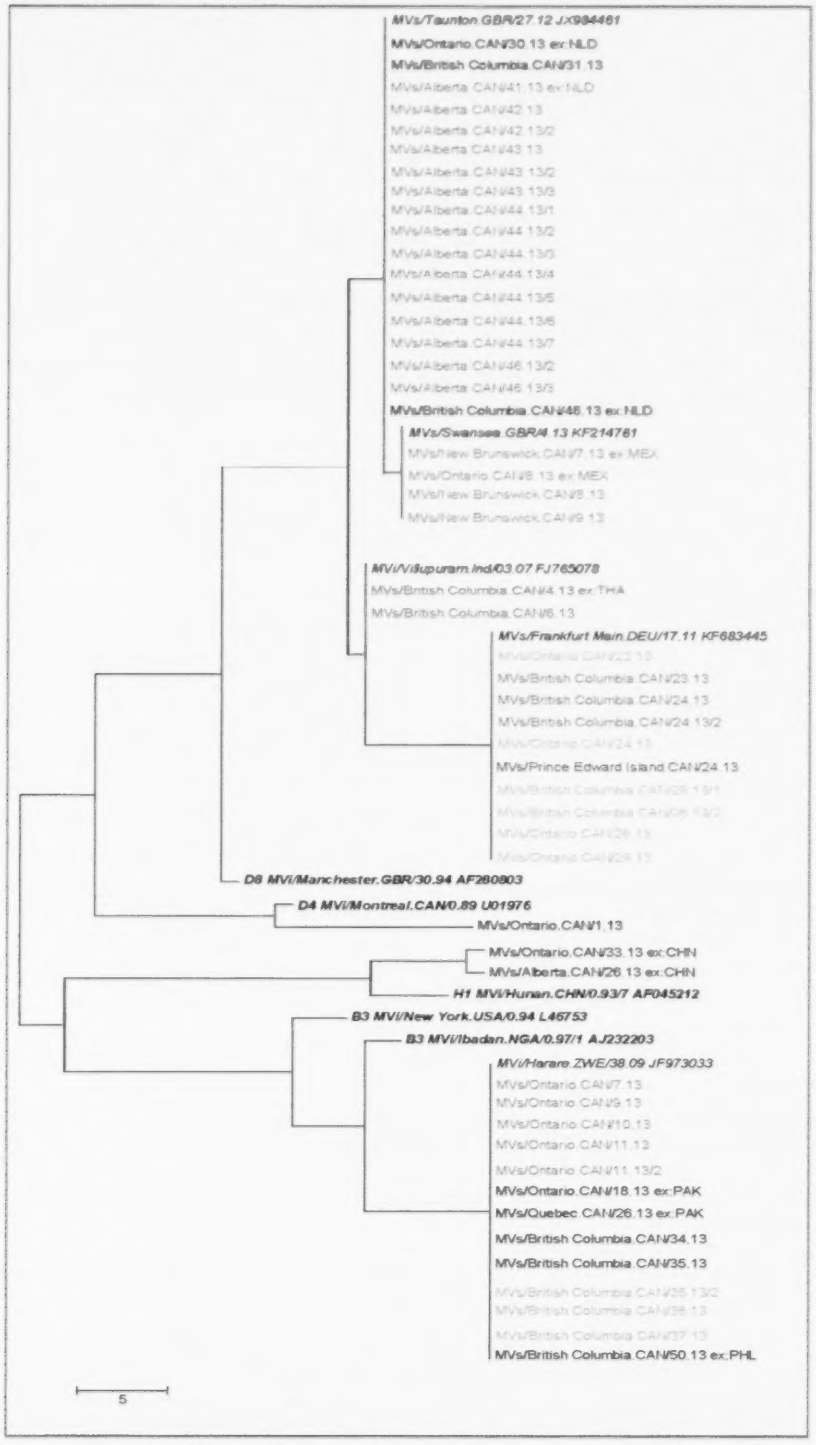
Molecular epidemiology

During 2013, specimens were available to determine the genotype for 50 of 83 (60.2%) reported cases of measles. Measles genotypes were D8 (n = 34), B3 (n = 13), H1 (n = 2) and D4 (n = 1).

Measles genotype D8 was detected in 34 cases and seven outbreaks (**Table 4**). In general, this genotype has been associated with endemic transmission in the Eastern Mediterranean region, primarily in the Southeast Asian region (16). The genotype D8 sequences identified could be further subdivided as four sequence variants (**Figure 2**): those that were identical to MVs/Taunton.GBR/27.12 (GenBank accession number JX984461) (n = 18), MVs/Frankfurt Main.DEU/17.11 (GenBank accession number KF683445) (n = 10), MVs/Swansea.GBR/4.13 (GenBank accession number KF214761) (n = 4) and MVi/Villupuram.Ind/03.07 (GenBank accession number FJ765078) (n = 2). The two cases that had sequences identical to MVi/Villupuram.Ind/03.07 were part of an outbreak that began as a result of an importation from Thailand (**Table 4**), where the sequence was circulating (GenBank accession numbers KC631635, KC631637-41). Measles sequences identical to MVs/Swansea.GBR/4.13 were detected in four cases, of which the two primary cases (MVs/New Brunswick.CAN/7.13 and MVs/Ontario.CAN/8.13, **Figure 2**) had returned from Mexico (**Table 4**). At the time, this sequence variant had been reported to the WHO measles sequence database, MeaNS (16), only from the UK (Kevin Brown, Public Health, England: personal communication, March 7, 2013), supporting the identification of a UK tourist as the index case.

Figure 2. Phylogenetic tree of measles N-450 sequences detected in Canada in 2013 (n = 50)

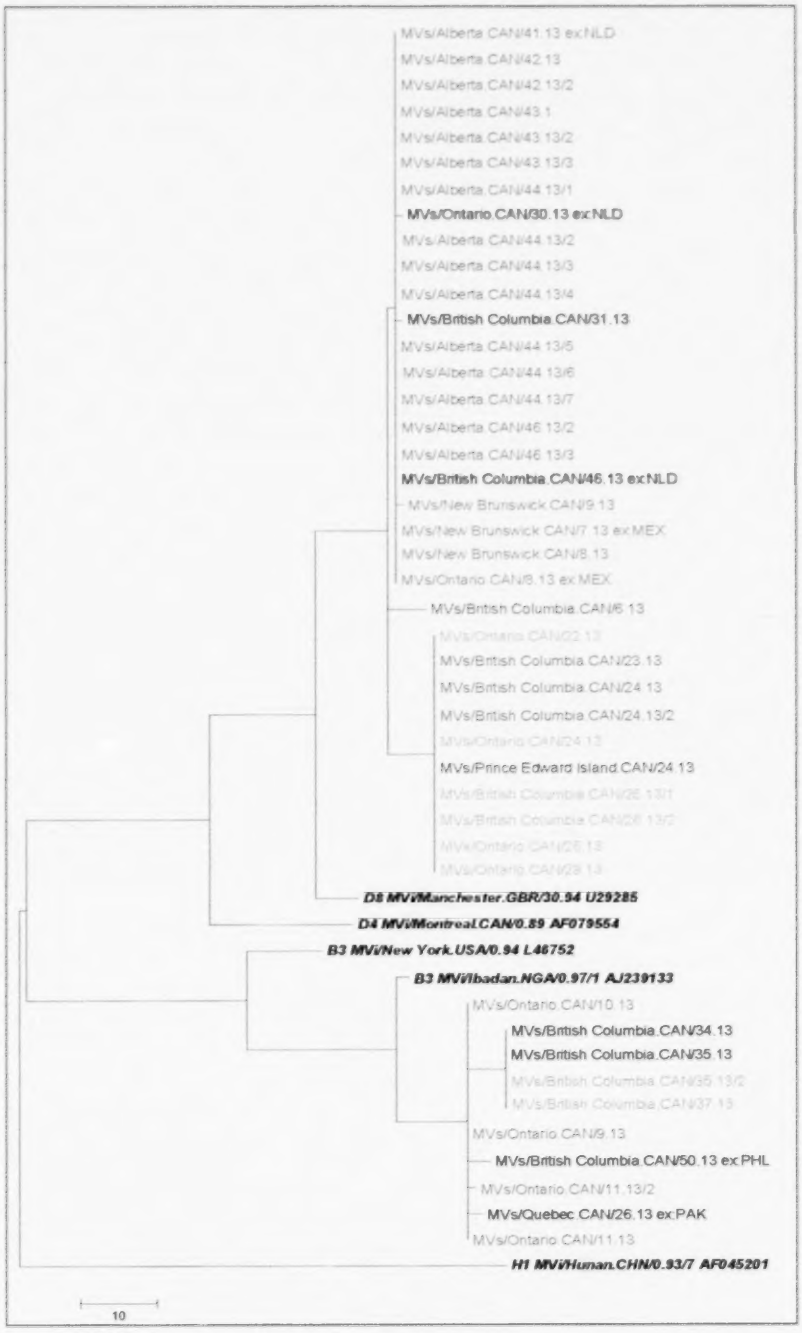
Each entry represents a sequence from an individual measles case. Phylogenetic trees demonstrate the relatedness of genetic sequences. Sequences on the same vertical line are identical. The length of horizontal lines separating sequences or branches of sequences is proportional to the number of differences (measured in single nucleotides) between the sequences (scale shown at the bottom left). WHO reference sequences (11) are shown in bold, italic font. Relevant sequence variants are shown in italics. These are identified within the WHO measles sequence database, MeaNS (accessible at http://www.who-measles.org/Public/Web_Front/sequence.php), and represent prevalent sequences within the database (11) Canadian sequences are shown in regular font and are identified by their WHO name, which indicates province and week of rash onset or specimen collection. Cases of imported virus are identified with "ex :< 3 letter country code>." Outbreaks are represented by colour fonts: sequences with the same colour, within the same genotype, are from the same outbreak.



In the months of June and July, four outbreaks occurred simultaneously in three provinces: Ontario, Prince Edward Island and British Columbia (n = 2), and sequences identical to MVs/Frankfurt Main.DEU/17.11 was identified from all four outbreaks (**Figure 2**). At the time of the outbreaks, the MVs/Frankfurt Main.DEU/17.11 sequence variant was circulating in the European region (GenBank accession numbers KF269094, KJ690815, KF290740, KF715463, KF269089) and detected in the United States (GenBank accession number KF385861). Sequencing of the secondary WHO genotyping region, the H gene, did not differentiate the four outbreaks (**Figure 3**).

Figure 3. Phylogenetic tree of measles H gene sequences detected in Canada in 2013 (n = 43)

WHO reference sequences (11) are shown in bold, italic font. Canadian sequences are shown in regular font and are identified by their WHO name, which indicates province and week of rash onset or specimen collection. Cases of imported virus are identified with "ex :< 3 letter country code>." Outbreaks are represented by colour fonts: sequences with the same colour, within the same genotype, are from the same outbreak.



The majority of the D8 sequences in 2013 were identical to the MVs/Taunton.GBR/27.12 sequence variant (n = 18), and all 18 were linked to the Netherlands (**Figure 2**), where the same sequence variant was associated with an ongoing outbreak (Susan Hahné, RIVM - Centre for Infectious Disease Control, the Netherlands: personal communication, June 12, 2013). Fifteen were associated with the Alberta outbreak, and the remaining three were unrelated importations. Two of the separate importations had distinct H gene sequences (MVs/Ontario.CAN/30.13 and MVs/British Columbia.CAN/31.13, **Figure 3**).

Measles genotype B3 was detected in 13 cases and was associated with two outbreaks whose origin could not be determined (**Table 4**, **Figure 2**). Genotype B3 has been associated with endemic transmission throughout the African region as well as a number of countries in the Eastern Mediterranean region (16). All Canadian B3 viruses sequenced were identical to the MVi/Harare.ZWE/38.09 sequence variant (GenBank accession number JF973033). At the time of the first outbreak in Ontario, this sequence variant was circulating in the Eastern Mediterranean region (GenBank accession numbers KC737549 and KF145165). Two sporadic cases were imported from Pakistan between outbreaks. At the time of the fourth outbreak in British Columbia, in the fall of 2013, this sequence variant was being reported from the Western Pacific and European regions in addition to the Eastern Mediterranean region (GenBank accession numbers KJ690812-4, KF468720, AB854746-7 and KF740427). At the end of the year, this sequence variant was also imported from the Philippines. Although all genotype B3 cases were identical at the primary genotyping region, the N-450 (**Figure 2**), the outbreaks and sporadic cases were distinguished by H gene sequencing (**Figure 3**).

Genotypes H1 (n = 2) and D4 (n = 1) were detected in three sporadic cases in 2013 (**Figure 2**). Genotype H1 was twice imported from the Western Pacific region, where it is endemic (16). Genotype D4 has been associated with endemic transmission in the Eastern Mediterranean, Southeast Asian and European regions (16). The source of the D4 case was unknown, although it was identical to a sequence variant circulating in the European region, MVs/Manchester.GBR/10.09 (GenBank accession numbers GQ370461, KC709569 and KF831037).

Summary of 2013 Canadian measles outbreaks

Nationally, an outbreak is defined as two or more cases of measles linked by person, place and time (17). In 2013, there were nine outbreaks composed of 71 cases. Of the remaining 12 non-outbreak-associated cases, seven were importations, and there was insufficient information to associate five cases with an existing outbreak.

Key characteristics of the reported outbreaks are included in **Table 4**. Outbreaks are presented in chronological order of rash onset of the index case. When the nature of the epidemiological links between outbreak-associated cases was not clearly described on the national case report form, this is specified in the table.

More than half (n = 42) of the outbreak-associated cases in 2013 was the result of a large outbreak in Alberta from October 16 to November 25 (duration: 40 days). This outbreak occurred in a non-immunizing community as a result of an importation from the Netherlands. The majority of the cases were male, median age was 13 years, and all cases were unimmunized. Additional details regarding this outbreak are provided elsewhere (18).

The following outbreak summary excludes the Alberta outbreak cases so as to not skew the results. The median number of cases per outbreak was 3.5 (the mean was similar at 3.6). The median duration from onset dates of the index case and last outbreak-associated cases was 14.5 days (or one incubation period from infection to rash onset) (19). The majority of the outbreaks (75.0%, n = 6) were limited to two generations of spread (median: 2). While outbreaks 3 and 4 (Ontario) were more extensive temporally, they were restricted to only five and six cases respectively. The origin of three outbreaks could not be determined.

Canadian measles in the global context

Of the 83 reported cases in 2013, 14.5% (n = 12) were classified as imported and 54.2% (n = 45) were epidemiologically linked to an imported case. Source of exposure could not be identified for 8.4% (n = 7), and 22.9% (n = 19) were epidemiologically linked to a case whose source of exposure was unknown.

The suspected country of exposure was identified for all importations. The 12 importations were acquired from the European Region (Austria/Italy/France [n = 1] and the Netherlands [n = 3]), the Western Pacific Region (China [n = 1], the Philippines [n = 1], and Taiwan [n = 1]), the Eastern Mediterranean Region (Pakistan [n = 2]), the Southeast Asian Region (Thailand [n = 1]) and the Region of the Americas (Mexico [n = 2]).

All importations were the result of a Canadian travelling to a measles-endemic country or being exposed to other travellers from measles-endemic countries (e.g. exposure to UK resident in Mexico). One importation was the result of a foreign national traveling to Canada while the infection was communicable.

Table 4. Summary of the nine measles outbreaks reported in Canada, 2013

#	Prov.	No. of cases	Onset date range (duration in days; number of generations)	Strain and sequence designation	Description
1	BC	2	January 31 to February 12 (13; 2 generations)	D8	• Index case imported the virus from Thailand. • Secondary case was a household contact.
2	NB and ON	4	February 19 to March 4 (14; 2 generations)	D8	• The index case was a traveller from the UK, who was visiting a resort in Mexico. • Two Canadians (one from ON and one from NB) were exposed to this measles case at the resort. • The ON resident was aged 30 to 39 years, with unknown immunization history. There were no secondary cases associated with the ON case. • The NB resident was aged 30 to 39 years and was unimmunized. • There were two secondary cases that occurred in Canada among unimmunized family members of the NB case. Both were aged 1 to 4 years.
3	ON	5	February 24 to March 21 (26; 3 generations)	B3	• This outbreak occurred in a childcare centre. • The source of exposure for the index case is unknown. • All cases were between the ages of 1 and 4 years. • Three cases (including the index) were unimmunized. Both immunized cases were up to date for age.
4	ON	6	June 8 to July 24 (47; 4 generations)	D8	• The three co-index cases had rash onset on June 8. • Co-index cases were unimmunized children aged 1 to 9 years who had recent travel history to British Columbia during their exposure period. • A secondary case was associated with the co-index cases, with suspected exposure in a health care setting: subsequent transmission resulted in a tertiary case in the same type of setting. • No exposure, other than co-index cases, was found for the 6th case (fourth generation).
5	PE	2	June 10 to June 22 (13; 2 generations)	D8	• Index case had recently travelled to Europe (Austria, Italy and France) where exposure was suspected. However, the D8 strain was not being reported in those countries at that time. • Secondary case was a sibling of the index case. Both cases were unimmunized and aged 10 to 19 years.

#	Prov.	No. of cases	Onset date range (duration in days; number of generations)	Strain and sequence designation	Description
6	BC	3	June 10 to June 26 (17; 2 generations)	D8	• Index case had recent travel outside of Canada to New York City, but epidemiological investigation also suggests possible exposure at Vancouver International Airport. • Two secondary cases were associated with the index case: the first was through workplace exposure and the nature of the second exposure was not provided. • Cases were aged 39 to 49 years. • Immunization history was known for 1 case (unimmunized, but considered up to date for age).
7	BC	4	June 24 to July 6 (13; 2 generations)	D8	• Index case was an unimmunized 25 to 29 year old, without history of travel. • Three secondary cases were associated with the index case. The nature of the exposure was not provided. • Secondary cases were aged 20 to 29 years. • One was up to date for age, one had received 1 documented dose of MMR, and the third had reported 2 undocumented doses of MMR.
8	BC	3	September 2 to September 16 (15; 2 generations)	B3	• Index case was an unimmunized < 1 year old, without history of travel. • There were two secondary cases: the first aged 1 to 4 years with no immunization history and the second aged 30 to 39 years with unknown immunization history.
9	AB	42	October 16 to November 25 (41; 4 generations)	D8	• Index case was exposed in the Netherlands. • Outbreak occurred in a non-immunizing community. • Cases ranged in age from < 1 year to 24 years.

MMR: measles mumps rubella vaccine.

Maintenance of measles elimination

PAHO's four essential criteria for measles elimination are listed in **Table 5** with a description of the indicator used to measure them and a summary of how the measles surveillance data support Canada's ongoing efforts to sustain its elimination status.

Table 5. Pan American Health Organization essential criteria for the elimination of measles

Criterion (17)	Indicator	Description
Verify the interruption of endemic measles cases for a period of at least 3 years from the last known endemic case, in the presence of high-quality surveillance	Zero cases of endemic transmission	*Criterion met* Documentation and verification of interruption of endemic measles in Canada from 1998 to 2011 are provided elsewhere (1,4). Molecular and epidemiological surveillance will continue through 2014 to ensure that there is no persistent circulation of the viral strains identified in 2013 for a period equal to or greater than 12 months.
Implement and maintain high-quality surveillance sensitive enough to detect imported and import-related cases	> 2 suspect cases per 100,000 population adequately investigated	*Criterion partially met* Data to support this indicator not available nationally. However, a national estimate was determined from the Measles and Rubella Surveillance pilot project data for the 2011 reporting year. The national measles-like illness investigation rate was 19 per 100,000 population. Note: this indicator was estimated during an outbreak year (Quebec 2011). Comparatively, the national estimate during the 2006 non-outbreak year was 12 per 100,000 population.
Verify the absence of endemic measles virus strains through viral surveillance	Measles genotype assessed in 80% of outbreaks	*Criterion met* The measles genotype was identified in 100% of the outbreaks in 2013.
Verify adequate immunization in the population	95% of population cohorts aged 1 to 40 years have received a measles-containing vaccine	*Criterion partially met* Data to support this indicator not available nationally for all age groups. The most recent national immunization coverage survey estimated first dose measles-containing vaccine coverage among 2 year olds to be 95.2% and second dose measles-containing vaccine coverage among 7 year olds to be 94.9% in 2011(6). However, according to epidemiological investigation of recent outbreaks and communication with provinces and territories we know that immunization coverage is heterogeneous across Canada, and there are areas with lower (and higher) coverage.

Discussion

This report summarizes the epidemiology of measles in Canada in 2013. Although measles has been eliminated in Canada, we continue to see cases of disease. While the 83 reported cases in 2013 represent the fifth highest number annually since 1998, eight of the nine outbreaks were highly restricted in their case distribution by either person or time (i.e. small number of cases or short outbreak duration). These findings suggest a possible combination of prompt and effective public health intervention and/or high immunization coverage among contacts. However, the large outbreak in the non-immunizing community in Alberta highlights the ongoing challenges in maintaining measles elimination in a country with heterogeneous immunization coverage.

In 2013, Canada had a number of importations, all from countries with endemic measles or outbreaks. All but one of these importations were by Canadians who acquired the disease while travelling abroad (the other was a foreign resident who travelled to Canada while communicable), emphasizing the continued importance of ensuring that all Canadians are adequately immunized, particularly before travelling.

Four measles genotypes were observed in 2013, D8 being the most prevalent and geographically represented (five provinces reported cases associated with this genotype).

Canada met or partially met all four criteria for measles elimination in 2013. Epidemiological and molecular measles surveillance was able to confirm the absence of circulation of any one dominant viral strain, although ongoing surveillance is required to ensure that this is sustained. While suspect case investigations are not captured at the national level, the proxy indicator measured through the Measles and Rubella Surveillance pilot project indicates an investigation rate in excess of the minimum required. Finally, despite national coverage estimates of 95%, pockets of people and groups within the population remain susceptible.

Limitations

Outcome information (e.g. duration of hospitalization, complications or death) on measles cases is not captured through national surveillance. Therefore, characterization of measles cases by severity of disease is not possible. Immunization status was unknown for 11% of cases, which limits our ability to fully understand the distribution of disease by immunization history.

The ability to collect detailed immunization histories of cases may be a challenge at the local level, where information is primarily gathered and submitted to provincial and then federal authorities for surveillance purposes. Improving the collection of immunization history in case reports should be explored.

References

(1) King A, Varughese P, De Serres G, Tipples GA, Waters J, Working Group on Measles Elimination. Measles elimination in Canada. *J Infect Dis*. 2004;189 Suppl 1:S236-42. doi: 10.1086/378499.

(2) Pan-American Health Organization (PAHO). Plan of Action: Documentation and verification of measles, rubella and congenital rubella syndrome elimination in the region of the Americas. Technical document. 2010.

(3) World Health Organization. Global measles and rubella strategic plan 2012-2020. http://www.refworks.com/refworks2/default.aspx?r=references|MainLayout::init.

(4) Public Health Agency of Canada. Elimination of measles, rubella and congenital rubella syndrome in Canada: Documentation and verification report. 2011.

(5) De Serres G, Markowski F, Toth E, et al. Largest measles epidemic in North America in a decade--Quebec, Canada, 2011: Contribution of susceptibility, serendipity, and superspreading events. *J Infect Dis*. 2013;207(6):990-998.

(6) Public Health Agency of Canada. Immunizaiton coverage in Canada (2002-2012). http://www.phac-aspc.gc.ca/im/nics-enva/icc-cvc-eng.php.

(7) van Boven M, Kretzschmar M, Wallinga J, O'Neill PD, Wichman O, Hahne S. Estimation of measles vaccine efficacy and critical vaccination coverage in a highly vaccinated population. *J R Soc Interface*. 2010;7(52):1537-1544.

(8) Public Health Agency of Canada. Counts of reported cases of measles over time in Canada, both sexes, all ages, from 1924 to 2012. http://dsol-smed.phac-aspc.gc.ca/dsol-smed/ndis/charts.php?c=pl.

(9) Public Health Agency of Canada. Case definitions for diseases under national surveillance. *CCDR*. 2009.

(10) World Health Organization. Standardization of the nomenclature for describing the genetic characteristics of wild-type measles viruses. *Weekly Epidemiological Record*. 1998;73:265.

(11) World Health Organization. Measles virus nomenclature update: 2012. *Weekly Epidemiological Record*. 2012;9(87):73.

(12) Tamura K, Peterson D, Peterson N, Stecher G, Nei M, Kumar S. Molecular evolutionary genetics analysis using maximum likelihood, evolutionary distance, and maximum parsimony methods. . *Molecular Biology and Evolution*. 2011;28:2731.

(13) SAS. Enterprise guide 5.1. 2013;5.1.

(14) Statistics Canada, demography division, demographic estimates section, July population estimates, 2013 final intercensal estimate.

(15) National Advisory Committee on Immunization (NACI). Statement on measles-mumps-rubella-varicella vaccine. 2010.

(16) Rota PA, Brown K, Mankertz A, et al. Global distribution of measles genotypes and measles molecular epidemiology. *Journal of Infectious Diseases*. 2011;204(Suppl1):8514.

(17) Public Health Agency of Canada. Guidelines for the prevention and control of measles outbreaks in Canada. *CCDR*. 2013;39.

(18) Kershaw T, Suttorp V, Simmonds K, St. Jean T. Outbreak of measles in a non-immunizing population, Alberta, october-november, 2013. *CCDR*. 2014;40-12: 219

(19) Heymann D, ed. *Control of communicable diseases manual*. 19th ed. Washington, DC: American Public Health Association; 2008.

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Conflicts of interest

There are no conflicts of interest to declare.

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Measles activity in Canada: January – June 2014

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Abstract

Since the beginning of 2014 to May 10, 103 cases of measles have been reported to the Public Health Agency of Canada from five provinces: British Columbia, Alberta, Saskatchewan, Manitoba and Ontario. Three factors contribute to this. First, Canadians travel more than they used to, increasing the risk in those who are not immunized of importing the disease into Canada. Second, there has been an increase in measles in countries that have high population exchange with Canada, including France (2011), the Netherlands (2013) and, most recently, the Philippines (2014). Finally, there is suboptimal immunization coverage in some areas across Canada. This year there have been 21 importations to May 10th, yet, despite how highly contagious measles is, only eight led to transmission within Canada. Strengthening immunization programs, maintaining heightened vigilance and continuing to achieve rapid containment of imported infections are essential for sustaining measles elimination.

Introduction

Despite the achievement of measles elimination in Canada, importations of measles cases and subsequent secondary spread are expected as long as measles remains endemic in other parts of the world. The following is a brief summary of Canadian measles activity in 2014.

Epidemiologic summary

Since the beginning of 2014 (epidemiologic week 1: December 30, 2013, to epidemiologic week 19: May 10, 2014), 103 cases of measles have been reported to the Public Health Agency of Canada (the Agency) through the Canadian Measles and Rubella Surveillance System. Cases have been reported from five provinces: British Columbia (n = 36), Alberta (n = 24), Saskatchewan (n = 16), Manitoba (n = 8) and Ontario (n = 19). Fraser Health Authority, British Columbia, has notified the Agency and the public of a large outbreak in the Fraser East area, where there are an estimated 423 cases; most of these have yet to be reported through the national surveillance system.

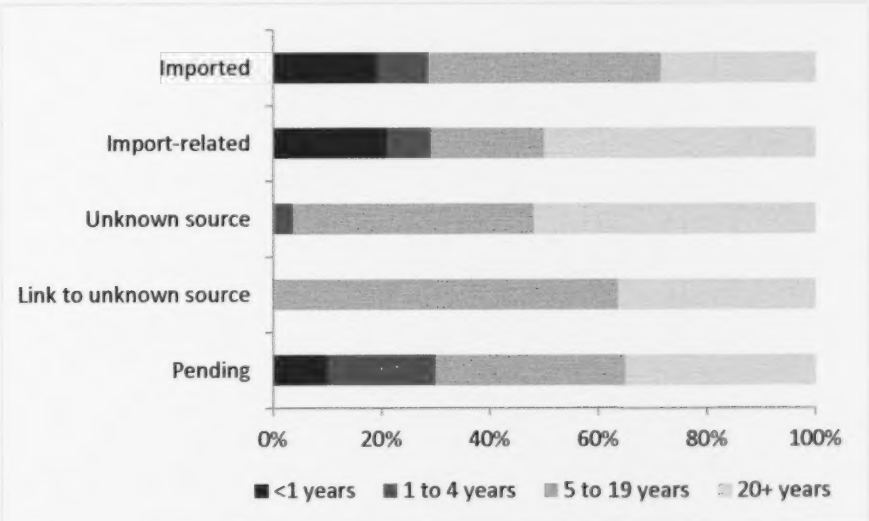
To date, 21 importations have been reported from six countries. The majority of the importations are from the Philippines (n = 15, 71%), where there has been a large outbreak of measles, but cases have also been imported from India (n = 2), the United States (n = 1), Thailand (n = 1), Pakistan (n = 1) and Italy/Amsterdam (n = 1). The number of measles importations to Canada has remained relatively stable over the years, with a median of 5 per year from 1998 to 2009. However, increases have been observed recently in 2010 (n = 10, Olympic year), 2011 (n = 29) and 2013 (n = 12). Changes in both travel patterns and the global incidence of measles activity are two contributing factors that may explain the increase in importations.

In 2000, Canadian residents took an estimated 4.5 million trips overseas while overseas visitors (non-residents) made 4.4 million trips to Canada (1). In 2012, Canadians took an estimated 11 million trips outside the country (excludes trips to the USA) (2), which represents a 2.5 fold increase in overseas travel. Comparison with the Canadian population increase of only 13% over the same period suggests that this travel increase is not only related to population growth (3).

A second contributor is increased measles incidence in countries that have high population exchange with Canada. For example, large outbreaks of measles in France (2011) (4), the Netherlands (2013) (5) and the Philippines (2014) (6) may account for the increase in measles importations to Canada.

Secondary spread of most importations has been limited in 2014. Of the 21 importations reported to May 10, eight have led to transmission within Canada. Of the five outbreaks that had concluded at the time of writing, the median duration between rash onset dates of the first and last cases was 20 days (range: 13 to 35), and the median number of cases was 3 (range 2 to 10). Of imported cases, the majority were unimmunized (n = 12, 57%) or had unknown immunization history (n = 4, 19%), the remainder having received one (n = 1, 5%) or two doses (n = 4, 19%) of measles-containing vaccine. The age distribution of measles cases by source of exposure is found in **Figure 1**.

Figure 1. Age distribution of confirmed measles cases by exposure source, Canada, December 30, 2013, to May 10, 2014 (n = 103)



Limitations

The information provided in this rapid communiqué is limited to what has been reported to the Agency through the Canadian Measles/Rubella Surveillance System or the Measles and Rubella Surveillance system pilot by May 10, 2014. Therefore, there may be inconsistencies with data reported by provinces and territories. A data audit is conducted annually with provinces and territories to validate measles data reported to the Agency.

Canada's *Plan of Action* for maintaining measles elimination

Canada does recognize that the threat of imported measles, combined with suboptimal immunization coverage in some areas, poses a risk of re-introduction and domestic transmission, as experienced during the 2011 measles outbreaks that threatened Canada's elimination status. Strengthening immunization programs, maintaining heightened vigilance and rapid containment of imported infections are essential for sustaining measles elimination.

For Canada to sustain measles and rubella elimination, all jurisdictions will need to continue to strengthen collaboration and support high-quality immunization programs. The Agency plans to consult with provincial and territorial partners and other experts, nationally and internationally, to develop and implement a multi-year *Plan of Action* building on earlier accomplishments, to ensure that measles elimination is sustained.

References

(1) King A, Varughese P, De Serres G, Tipples GA, Waters J, Working Group on Measles Elimination. Measles elimination in Canada. *J Infect Dis*. 2004;189 Suppl 1:S236-42. doi: 10.1086/378499.

(2) Statistics Canada. International travel survey, Canadian residents 2008-2012, custom extract for the Public Health Agency of Canada. 2014.

(3) Statistics Canada, demography division, demographic estimates section, July population estimates, 2011 final intercensal estimate.

(4) World Health Organization European Region. Centralized information system for infectious diseases. http://data.euro.who.int/cisid/.

(5) Knol MJ, Urbanus AT, Swart EM, et al. Large ongoing measles outbreak in a religious community in the Netherlands since May 2013. *Eurosurveillance*. 2013;18(36).

(6) World Health Organization Western Pacific Region. Measles-rubella bulletin April 2014. http://www.wpro.who.int/immunization/documents/MRBulletinVol8Issue04.pdf?ua=1.

Measles-containing vaccination rates in southern Alberta

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Abstract

Background: Southern Alberta is home to many unique homogeneous communities that typically educate their children in private schools. A number of these communities do not promote immunization as a preventive public health measure, although the reasons behind this vary. People within these communities keep themselves somewhat secluded from other populations and thus do not benefit from overall herd immunity. This has led to frequent outbreaks of vaccine-preventable diseases in private schools affiliated with these homogeneous religious communities.

Objective: To report on low immunization rates of measles, mumps, rubella (MMR) and MMR-varicella in southern Alberta communities and schools and to compare the epidemiology of immunization rates in certain vulnerable communities with those of same-age cohorts in South Zone communities.

Methods: The analysis includes immunization data at the individual level submitted to the provincial immunization repository, Immunization and Adverse Reactions to Immunization, and the Alberta Health Services Meditech module between January 1, 2013, and June 30, 2013.

Results: Heterogeneity of immunization status was found among communities and among schools. The status of two year old children up to date on immunizations ranged from 46.6% in Fort Macleod to 71.9% in Oyen, with a mean of 57.3 children in every 100 up to date. By age seven, the mean percentage of immunized children in southern Alberta was 77.6%, ranging from 57.8% in Picture Butte to 94.6% in Oyen. Immunization status among schools ranged from 17% to 100%, with a mean of 89.3% of children fully immunized and a median of 91% immunized.

Conclusion: There is heterogeneity of immunization uptake for childhood measles-containing vaccine by community and by school in southern Alberta. This study highlights that the location of the school may not align with geographic community as it pertains to immunization rates. Analysis of childhood immunization data at both community and school level is important in understanding the risks of vaccine-preventable illness spread in a given geographic region, such as Alberta South Zone. Data from this study can be used to inform specific interventions required to improve immunization coverage rates in these unique homogeneous cultural communities and their respective schools, and to decrease the risk of measles transmission in Southern Alberta.

Introduction

Measles is a highly communicable disease caused by the direct transfer of the measles virus by respiratory droplets or small-particle aerosols to human hosts. Particles remain suspended in air for up to two hours, and transmission of the virus is best prevented by active immunization with measles vaccine (1). In order to achieve successful herd immunity for measles disease, Alberta Health has set the target of 98% for children of two years of age to have received one dose of measles-containing vaccine, and 99% of children by 7 years to have received two doses of measles-containing vaccine (2). Preventing transmission remains dependent on a number of factors, such as a highly immunogenic vaccine; random mixing of a heterogeneous population; and consistent vaccination coverage among groups (3). The measles vaccine is highly effective, a single dose conferring 85%-95% immunity and a booster dose raising the effectiveness to almost 100% (4). Within a given population, some

individuals will choose not to immunize. Random mixing refers to the importance of these non-immune individuals being incorporated into the portion of the population that is immunized, where they can be protected from acquiring disease through herd immunity. Herd immunity protects communities from measles outbreak by preventing the rapid spread of the virus. Although the number of children infected with and dying from measles per annum has decreased drastically since the routine administration of the measles vaccine, the disease still remains a public health problem and is returning to countries from which it was once thought to be eliminated or nearly eliminated (1,5-7). Strong religious or cultural beliefs against immunization, increasing travel across borders and continents, homogeneous subpopulations with insufficient vaccination coverage and lack of information or misinformation about vaccine safety are contributing to the re-emergence of measles (3, 7).

The most southern part of Alberta, the area south of Calgary, is one of five geographic areas within Alberta where health care is provided through Alberta Health Services (AHS). There are 17 public health offices (PHOs) in South Zone where children receive immunizations. Within South Zone there are various socially isolated communities with low immunization uptake for varying reasons (8). The largest of these communities is represented by the Netherlands Reformed Congregation, Low German Speaking Mennonite communities, and some Hutterite colonies. Each of them shares unique religious and/or cultural beliefs, and they are highly interconnected within their own community, resulting in minimal random mixing with the rest of the population in their geographic area. The majority of children from these communities are transported by school bus to private schools or are home-schooled, and participate in extracurricular activities such as sports and church primarily within their tight-knit social networks. Individuals have strong ties to countries such as the Netherlands, Mexico and South America, as well as other similar cultural settlements across North America. Travel to related communities with low immunization rates poses a risk of importation of vaccine-preventable disease to southern Alberta and potential high risk of spread. Although within some of these conservative religious communities there are individuals and families beginning to accept immunization, many still do not immunize their children. Cultural norms and expectations make it challenging for individuals to make informed decisions about immunization (8-10).

Historically in southern Alberta, there are frequent vaccine-preventable disease outbreaks. For example, over the past 20 years pertussis outbreaks have occurred every 3 to 5 years. The last large pertussis outbreaks in this area were in 2009 and 2012, in different religious communities. Analysis of the 2009 outbreak demonstrated that the outbreak originated in one of the private schools with very low immunization rates, and that there was ongoing transmission over an 11 month period within this school. Two months into the outbreak, pertussis illness spread to public schools in the geographic communities where children from the index school reside. Because of immunization rates that were closer to reaching herd immunity targets in public community schools, there was minimal transmission in these schools.

The objective of this article is to report on low MMR/MMR-V immunization rates in southern Alberta communities and schools, and to compare the epidemiology of immunization rates in certain vulnerable communities with that of similar age cohorts in the general population. Analysis of immunization rates in the geographic areas serviced by local PHOs are conducted to determine which areas have the highest and lowest uptake and the conclusions will inform future efforts to determine the best methods of intervention and education.

Methods

Measles, mumps, rubella and, more recently, varicella immunization in Canada is provided through a single vaccine (MMR or MMR-V) delivered in two doses (11). In Alberta, all childhood immunization is delivered by Alberta Health Services Public Health at public health offices and in school settings, with immunization policy and directives provided by Alberta Health. According to the Alberta Health routine immunization schedule, children in Alberta receive their first dose at 1 year and their second at 4-6 years (11). Individual-level data on immunizations in Alberta South Zone are entered at the point of care into the Meditech immunization module. Meditech data are submitted to the Alberta Health provincial repository, known as Imm/ARI (Immunization and Adverse Reactions to Immunization). In this study, community immunization data were obtained from the Imm/Ari database using postal codes, and school-level data were obtained from Meditech. Only children attending public and private schools were included; home-schooled children were not captured in the analysis. Schools were grouped by postal code into the PHOs used to analyze community immunization data. Two year

old children with zero doses of vaccine were defined as unimmunized, and those with one dose were considered up to date on their immunizations. Seven year old children with zero doses (unimmunized) were considered as potentially those whose parents refused immunization; children with a single dose were categorized as partially immune; and those with two doses (up to date) were considered fully immunized.

Immunization data not accurately captured in this analysis were data for children who had been immunized in other jurisdictions in Alberta or out of province and who had not yet had their records updated by public health. These included First Nations children who received their immunizations through federally administered programs. Given this, immunization data for the towns of Standoff and Brocket, within two First Nations communities, were not included in the analysis. Additionally, immunization rates in Cardston need to be interpreted with caution as the postal codes for Cardston include areas where children receive immunization through the federal program.

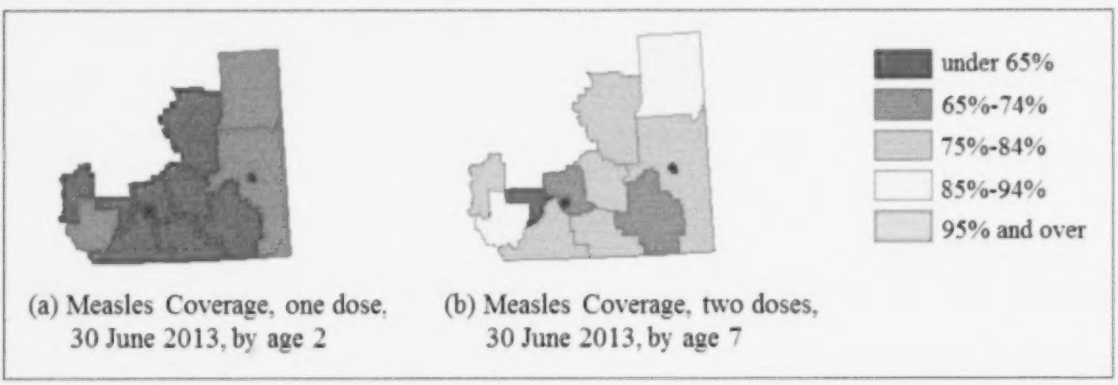
Data analysis

Immunization rates per 100 population at the community level were calculated using available denominators and demographic data from Imm/ARI. Population data by PHO for children who were two and children who were seven by June 30, 2013, were used. The ages two and seven years were chosen on the basis of the routine immunization schedule (9); these ages allow a year of leeway for children to receive their doses on schedule. We compared number of doses of vaccine that children had received by age two (zero doses or at least one dose) and by age seven (zero doses, one dose or at least two doses) in each PHO catchment area. The number of children for each cohort (age 2 and 7 years) with zero, one or two doses was included in the numerator and the total number of children in that age group was the denominator. The quotient was multiplied by 100 to obtain incidence per 100 children. Immunization rates by school were similarly calculated using data from the Meditech module for children attending public and private schools who were seven by June 30, 2013.

Results

Findings indicate that 42.8% of two year old children in the AHS South Zone were unimmunized and 57.3% were up to date on their immunizations as of June 30, 2013. At that time, 14.3% of seven year old children were unimmunized, 8.1% were partially immunized, and 77.6% were fully immunized. Immunization rates by age and community are shown in **Figures 1** and **2**.

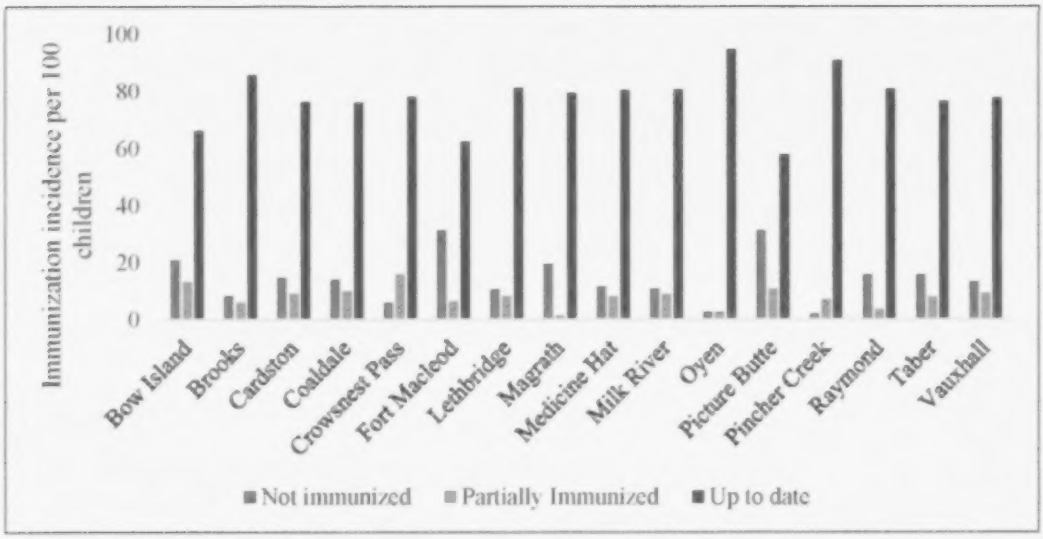
Figure 1. Immunization status of children by age two and by age seven in AHS South Zone



(a) Measles Coverage, one dose, 30 June 2013, by age 2

(b) Measles Coverage, two doses, 30 June 2013, by age 7

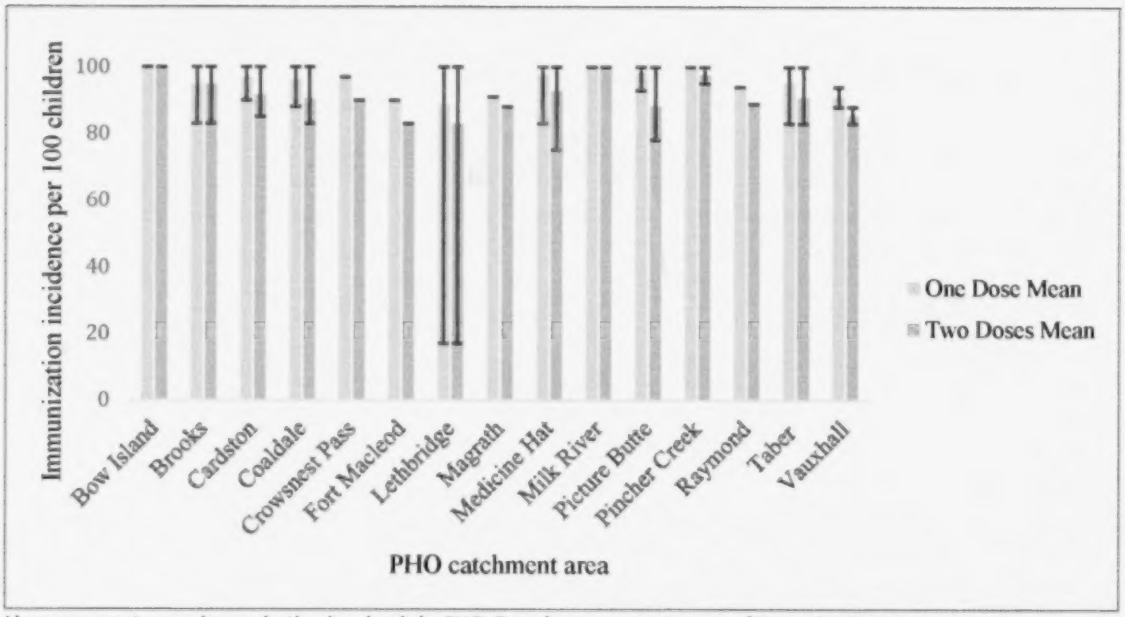
Figure 2. Immunization incidence rates per 100 eligible population by age seven in AHS South Zone Public Health Office catchment area



Examining immunization rates by PHO geographic area, we discovered that more than half of two year olds in Fort Macleod (53.4%), Picture Butte (64.9%) and Vauxhall (59.5%) were unimmunized. The highest incidence rate of children up to date on their vaccinations by age two was in Oyen, at 71.9%, and the majority of full immunization in the PHOs ranged from 56.0% in Raymond to 69.8% in Medicine Hat. By age seven, the incidence rate of non-immune children was high in Bow Island (20.8%), Fort Macleod (31.2%) and Picture Butte (31.3%). These PHO areas also had low rates of fully immunized seven year old children, at 66.0%, 62.3% and 57.8% respectively. The incidence rates of fully immunized children were above 90% in only two PHOs, Pincher Creek (90.7%) and Oyen (94.6%). Over 80% of seven year olds were up to date on their immunizations in Brooks, Lethbridge, Medicine Hat, Milk River and Raymond.

Schools with a seven year old population of five or fewer students were omitted, as was Ralston School in the Medicine Hat PHO, resulting in 80 schools available for analysis. Oyen was removed from analysis as all schools in this PHO contained fewer than five children aged seven. The mean incidence of partial immunization was 94.4 children per 100 eligible (SD = 11.1), with a median immunization incidence of 100% and a range of 17% to 100%. Results for the incidence of fully immunized children were similar, with a mean of 90% immunization (SD = 12.1). The median for fully immunized children in all schools was less than that for partial immunization, at 91%, but the range was the same (17% to 100%). When analyzed by PHO, Fort Macleod (n = 1), Lethbridge (n = 23, range = 17%-100%), Vauxhall (n = 2, range = 83%-88%) and Picture Butte (n = 4, range = 78%-100%) had the lowest means for full immunization at 83.0%, 83.1%, 85.5% and 88.3% respectively. Results are shown in **Figure 3**.

Figure 3. Immunization incidence rates per 100 eligible population by age seven in AHS South Zone public and private schools by PHO catchment area



Lines represent mean immunization in schools by PHO, Error bars represent range of immunization status across schools

Discussion

The results of this study show immunization coverage with measles-containing vaccine to be far below the accepted 90%-95% required for herd immunity in the majority of South Zone communities, and well below the Alberta population targets (3, 5). We found that only two communities in southern Alberta had vaccination rates among seven year olds approaching the Alberta Health target of 99%. In further exploration of measles immunization rates at a school level, there is significant heterogeneity among schools for this same 7 year old cohort. School measles immunization rates do not align with the respective community immunization rates. There are two primary reasons for this. First, schools with low immunization rates for measles disease are primarily private schools, where children from specific cultural/religious communities are transported from broad geographic catchment areas by school bus. As an example, the 7 year old immunization rate for the four schools in the Picture Butte area has a range of 78.0% and median of 87.5% This community is also one of the locations of residence of children who attend a private school in the Lethbridge PHO catchment area with an immunization rate of 17% for this age cohort. A second reason to explain the lack of consistency between community and school data is the fact that the community-level data additionally include home-schooled children, who may or may not be immunized. For example, there are a number of Low German Speaking Mennonite home schools where the majority of children are not immunized and where families are quite transient. These schools are not included in the data analysis since public health does not receive school registration lists and does not immunize in these schools.

Awareness of immunization rates by community and by school provides information on the risk of spread of a vaccine-preventable illness such as measles. A school with low immunization rates is a likely place for an outbreak to occur (12). If unimmunized exposed and/or symptomatic children travel from a school to their home communities, measles virus can further spread to vulnerable individuals within these communities. As there are no geographic locations within the South Zone with a high enough immunization rate to confer immunity to the entire population (**Figure 3**), it becomes increasingly possible for a highly contagious virus such as measles to spread across the South Zone and other parts of the province (3, 13).

This study did not investigate the reasons for low immunization rates at either the community or school level, such as religious beliefs, educational gaps, access to immunization. However, this information could be used in conjunction with previous studies that have explored perspectives of non-immunizing individuals in southern Alberta to inform targeted methods of intervention (8). Furthermore, further research is recommended to identify acceptable methods of school-level intervention for the private schools with low immunization rates. Monitoring of change in immunization rates over time by South Zone community and by school is critical to measuring the impact of interventions.

Conclusion

There is heterogeneity of immunization uptake for childhood measles-containing vaccine by community and by school in southern Alberta. This study highlights that location of school may not align with geographic community as it pertains to immunization rates. Childhood immunization data analysis at both the community and school level is important in understanding the risks of vaccine-preventable illness spread in a given geographic region such as Alberta South Zone. Data from this study can be used to inform specific interventions required to improve immunization coverage rates in these unique homogeneous communities and their respective schools, and to decrease the risk of measles transmission in southern Alberta.

References

(1) Moss WJ, Griffin DE. Measles. *The Lancet* 2012; 379:153-164.

(2) Alberta Immunization Strategy 2007-2017 http://www.health.alberta.ca/documents/Immunization-Strategy-07.pdf

(3) Rashid H, Khandaker G, Boy R. Vaccination and herd immunity: what more do we know? *Curr Opin Infect Dis* 2012; 25:243-249.

(4) National Advisory Committee on Immunization. Canadian Immunization Guide: Part 4 – Active Vaccines. *Ottawa: Public Health Agency of Canada* 2012. http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meas-roug-eng.php

(5) Lievano F, Galea SA, Thornton M, *et al.* Measles, mumps, and rubella virus vaccine (M-M-R™II): a review of 32 years of clinical and postmarketing experience. *Vaccine* 2012; 30(48):6918-6926.

(6) Leuridan E, Sabbe M, Van Damme P. Measles outbreak in Europe: susceptibility of infants too young to be immunized. *Vaccine* 2012; 30:5905-5913.

(7) Maltezou HC, Wicker S. Measles in health-care settings. *Am J Infect Control* 2013; 41:661-663.

(8) Kulig JC, Meyer CJ, Hill SA, Handley CE, Lichtenberger SM, Myck DM. Refusals and delay of immunization within southwest Alberta. *Canadian Journal of Public Health* 2002: 93(2), 109-112.

(9) Muscat, M. Who gets measles in Europe? *J Infect Dis* 2011: 204 (Suppl 1), S353-S365

(10) Knol MJ, Urbanus AT, Swart EM, Mollema L, Ruijs WL, van Binnendijk RS, te Wierik MJ, de Melker HE, Timen A, Hahné SJ. Large ongoing measles outbreak in a religious community in the Netherlands since May 2013 . *Euro Surveill.* 2013;18(36):pii=20580.

(11) Alberta Health Services. Routine Immunization Schedule. http://www.health.alberta.ca/health-info/imm-routine-schedule.html10.

(12) Lee BR, Feaver SL, Miller CA, Hedberg CW, Ehresmann KR. An elementary school outbreak of varicella attributed to vaccine failure: policy implications. *J Infect Dis* 2004: 190(3), 477-483.

(13) Parker AA, Staggs W, Dayan GH, *et al.* Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. *N Engl J Med* 2006; 355:447-455.

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Conflict of Interest

No conflicts of interest to declare.

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Outbreak of measles in a non-immunizing population, Alberta 2013

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Abstract

Background: An outbreak of measles was declared in southern Alberta on October 18, 2013, after a case had been reported to the local public health unit in a non-immunized teenager with recent travel to the Netherlands. The teenager had had contact with a large number of unimmunized people while infectious; therefore, the risk of spread was high. The potential for an outbreak of measles in this area had been identified by the lead Medical Officer of Health for South Zone, and planning for an outbreak had begun in August 2013.

Methods: Several public health measures were implemented to control the outbreak: mass immunization clinics; an outbreak dose of measles mumps and rubella (MMR) vaccine for infants 6-12 months old; communication within the affected and surrounding communities; a dedicated measles hotline; a Mobile Measles Assessment Team; and a Measles Assessment Centre.

Results: A total of 42 confirmed cases were identified during the outbreak between October 16 and November 25. Just over half the cases were male (52.4%). The average age was 12 (range < 1 to 24 years) and the median age 13 years. There was one hospitalization, and no deaths occurred. All cases were unimmunized. Cases were located in five communities immediately surrounding Lethbridge. All but two cases were epidemiologically linked within 10 households.

Conclusion: The planning that occurred before the outbreak was essential in containing the outbreak to 10 households. To prevent future outbreaks of measles, exploring strategies for increasing immunization coverage rates in unimmunized populations is essential. When immunization acceptance is not uniform, other public health strategies should be planned for and implemented in order to prevent additional spread.

Introduction

Measles is a highly contagious virus spread through airborne transmission with a greater than 90% secondary attack rate among susceptible individuals (1). Approximately 30% of measles cases experience one or more complications, and in developed countries 1-2 cases per 1,000 will result in death (1, 2). Measles is vaccine-preventable: a single dose of measles-containing vaccine is 85%-95% effective, and a second dose raises efficacy to almost 100% (1). In Alberta, the childhood schedule for a measles vaccine is one dose at 12 months of age and a second dose at 4-6 years of age. The last significant outbreaks of measles in Alberta occurred in 1997 (242 cases), 1999 (17 cases) and 2000 (123 cases).

Health services (including public health services) in Alberta are delivered by Alberta Health Services, which is divided into five zones. The South Zone, the area south of Calgary that includes Lethbridge and Medicine Hat, is composed of diverse cultural groups, many of whom do not support immunization and have historically experienced outbreaks of vaccine-preventable disease. In the County of Lethbridge, the area immediately to the west, north and east of Lethbridge, the last outbreak of measles was in 1997, leaving a large cohort of children born after 1997 not immune to measles disease by natural exposure or immunization. A large demographic group within the County of Lethbridge are families with strong ties to the Netherlands, where, since May 2013, a large-scale outbreak of measles has been occurring in a religious community known to object to immunization

(3, 4). The lead Medical Officer of Health (MOH) for South Zone recognized the risk of measles importation to southern Alberta and began planning for a potential outbreak in August 2013.

This measles preparedness phase used emergency disaster management principles, including use of the incident command system. A number of key strategies and plans were completed for South Zone during this time: 1) implementation of the 2012 National Advisory Committee on Immunization guidelines for measles immunization of health care workers; 2) broad communication to external stakeholders and the public to raise awareness of the risk of measles, promote immunization and educate about measures to minimize transmission for those who do not immunize; 3) engagement between local public health and church leaders, physicians and school administrators; and 4) development of a measles assessment centre plan, triage tools and completion of an inventory and retro-fit of rooms to meet negative pressure standards as per the Canadian Standards Association.

This planning proved to be valuable, because on October 16, 2013, local public health was notified of a suspect measles case in Lethbridge County in a non-immunized teenager with recent travel to the Netherlands. The case had classic measles presentation, with coryza and cough (October 9), followed by fever (October 11) and a maculopapular rash (October 16). Because of information provided to families during the measles planning period, the family was aware of the need to report to public health. This enabled public health officials to obtain laboratory specimens in the client's home on October 16, minimizing the risk of exposure in health care settings. Laboratory results confirmed measles on October 18. The case was known to have interacted, while infected, with a large number of people at a public sporting event, church, school and family events during the Thanksgiving holiday. The majority of these contacts were members of a religious community in which immunization is generally not accepted. On the basis of the risk of spread in a non-immunizing community, an outbreak of measles was declared in South Zone on October 18, 2013.

In this report we present the details of the outbreak, including its epidemiology and the public health measures that were implemented. Lessons learned will be provided for other jurisdictions to consider when dealing with outbreaks of measles, specifically in non-immunizing populations.

Methods

The outbreak of measles was declared on October 18, 2013, and was confirmed to be over on January 6, 2014. Emergency operations centres were opened in South Zone and at Alberta Health Services and Alberta Health. All three emergency operations centres used principles of the incident command system, which allowed streamlined collaboration and communication among the organizations.

Case finding and data collection activities

The case definition for measles had been previously established by Alberta Health in the Public Health Notifiable Disease Management Guidelines (5). One clarification was made to the application of the case definition, which was that clinical illness must be evaluated by a health care professional, including public health, and could not be self-reported. Case definitions for confirmed, probable and suspect cases can be seen in **Table 1**.

Table1. Confirmed, probable and suspect case definitions for measles in Alberta

Case classification	Definition
Confirmed	A laboratory confirmation of infection in the absence of recent immunization with measles-containing vaccine, meeting one of the following criteria: • Detection of measles virus nucleic acid (e.g. real-time polymerase chain reaction) in a clinical specimen; • Seroconversion or a significant (i.e. fourfold or greater) rise in measles IgG titre between acute and convalescent sera by any standard serologic assay; • Positive serologic test for measles IgM antibody in a person who is either epidemiologically linked to a laboratory-confirmed case or has recently travelled to an area of known measles activity; • Isolation of measles virus from a clinical specimen (e.g. nasopharyngeal swab, urine); or

Case classification	Definition
	• Clinical illness* in a person who is epidemiologically linked to a laboratory-confirmed case.
Probable	Clinical illness meeting one of the following criteria: • In the absence of both appropriate laboratory tests and an epidemiological link to a laboratory-confirmed case; or • In a person who has recently travelled to an area of known measles activity.
Suspect	Clinical illness even when the maculopapular rash has been present for less than three days.

* Clinical illness is characterized by all of the following features: 1) fever 38.3°C or greater; 2) cough, coryza or conjunctivitis; and 3) generalized maculopapular rash for at least three days.

Contact tracing was done with all known contacts of the index case and subsequent cases, but because of the public events the index case had attended there was also broad community exposure. As a result, media releases were issued in South Zone and throughout the province to provide information on measles for members of the public, and a dedicated 'phone line was set up for public inquiries. All suspect cases were investigated by public health and, once confirmed, were reported on a notifiable disease report form and entered into the Communicable Disease and Outbreak Management system.

Epidemiological analysis

Descriptive epidemiology was completed for the cases on an ongoing basis. Social network analysis was completed on the cases and household contacts of 10 epidemiologically linked families using Pajek software. To complete this analysis, household contact lists were extracted from the case management database for each case and included contacts' immunization history and whether they had a history of disease. In addition, a list of close contacts of cases was extracted to visualize known relationships between cases in the network. The overall and non-immunized household attack rates were calculated for the epidemiologically linked families. Five individuals were excluded from both attack rate calculations: the index case, the co-primary case (probable case), an individual who declined further public health follow-up (case status could not be confirmed) and two individuals who had received two doses of measles-containing vaccine. Twenty-one individuals were excluded from the non-immunized attack rate calculation: 20 who had a self-reported history of disease and one who had had one dose of measles-containing vaccine.

Laboratory methods

The Alberta Provincial Laboratory performed molecular testing, by real-time polymerase chain reaction (RT-PCR), on nasopharyngeal swabs and urine, and conducted serologic testing for measles antibody on blood. Samples testing positive by the measles PCR were referred to the National Microbiology Laboratory in Winnipeg for confirmation and genotyping of the virus. Serologic confirmation was based upon the detection of measles IgM antibody in the acute sample of blood or seroconversion of measles IgG antibody between acute and convalescent samples.

Public health measures

The outbreak teams reacted quickly and efficiently to implement key public health measures, most of which had been planned during the measles preparedness phase, in order to contain the outbreak of measles. Key measures included the following.

Communication: Timely, transparent, consistent and frequent communication to internal and external stakeholders through traditional and social media was essential during the outbreak. Upon confirmation of the

index case, the local MOH immediately met with clergy/pastors and school leaders to inform them and encourage implementation of measures to minimize further spread of disease.

Dedicated measles hotline: A dedicated 'phone line staffed 24/7 during the outbreak was established to address public inquiries. Any 'phone calls about measles received by Health Link, Alberta's telephone service providing free nurse advice and health information to Albertans, were directed to the hotline. The hotline was also available to physicians and served to provide direct triage for the Mobile Measles Assessment Team.

Mobile Measles Assessment Team: The Mobile Measles Assessment Team was established to provide 24/7 assessment of potential cases of measles in the community and divert this population from health care settings. The teams, comprising paramedics and home care nurses in 'phone consultation with Emergency Department physicians, would go to suspected cases' homes to assess individuals for measles, obtain laboratory specimens and provide self-care instructions when indicated.

Measles Assessment Centre: A Measles Assessment Centre was set up outside the Emergency Department of the regional hospital using a Portable Isolation Containment System tent for both assessment and treatment of measles patients. In order to reduce the likelihood of measles transmission in health care settings, and because of the limited availability of negative pressure rooms, the Portable Isolation Containment System tent was a vital public health measure.

Immunization clinics and outbreak doses: Eight public mass immunization clinics were offered in South Zone, and an outbreak dose of MMR was offered to infants 6-12 months of age at well-baby clinics and at the mass clinics.

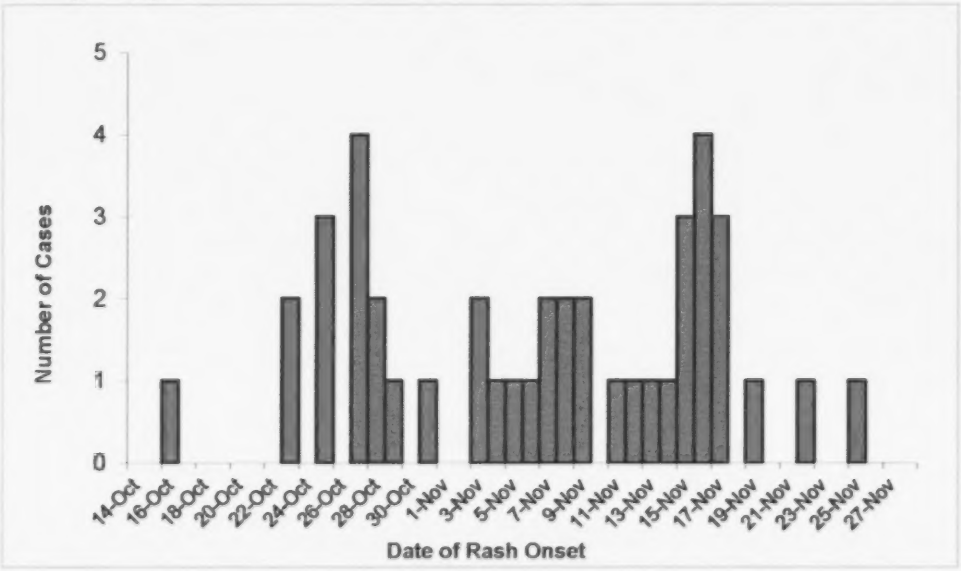
Quarantine and exclusion: Contacts of cases who were unimmunized were encouraged to self-exclude from school or work until 21 days after the last case was detected in their household. Cases were asked to self-quarantine to their home until they were no longer considered infectious. Quarantine orders were only written upon request, usually for work purposes.

Results

Descriptive epidemiology

A total of 43 cases (42 confirmed cases and 1 probable case) were identified during the outbreak. Rash onset for the index case occurred on October 16, and rash onset for the last case occurred on November 25 (**Figure 1**).

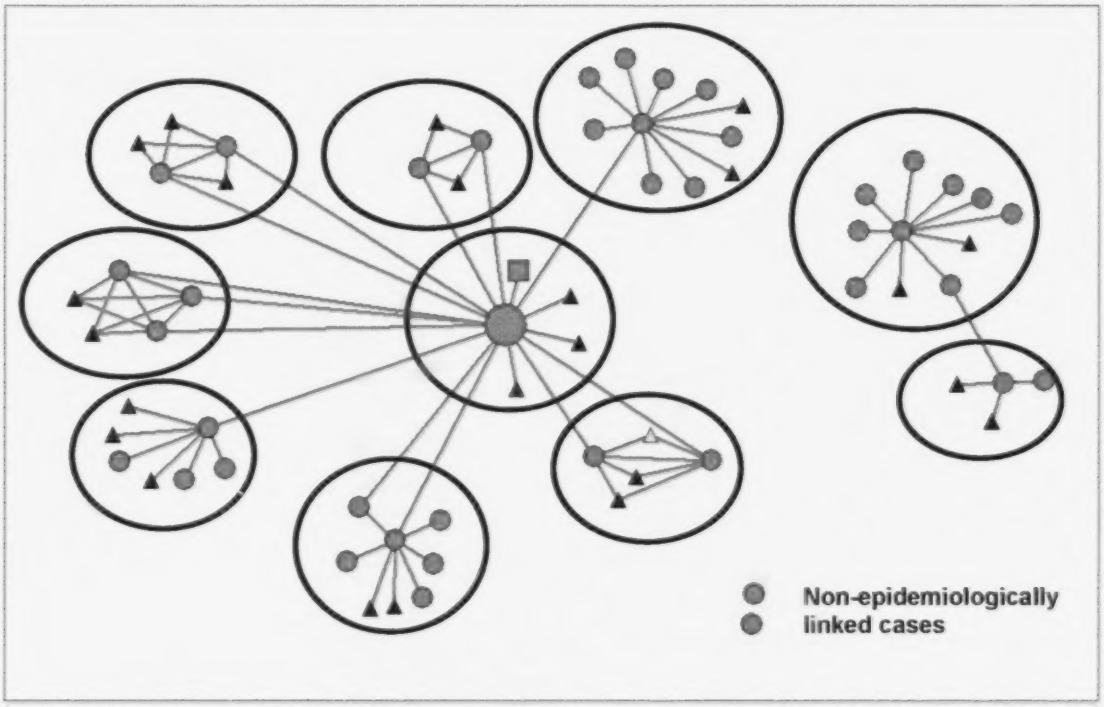
Figure1. Confirmed cases of measles in Alberta by date of rash onset, October 16-November 25, 2013 (n = 42)



Just over half of the confirmed cases were male (52.4%). The average age was 12 (range < 1 to 24 years) and the median age 13 years. Six complications were reported: two cases of pneumonia, three cases of dehydration and one case of otitis media. One of the pneumonia cases required hospitalization. No deaths were associated with this outbreak. Cases were located in five communities immediately surrounding Lethbridge. All cases were unimmunized.

All but two cases were contained to 10 households. These latter two cases had no direct epidemiological link: one resided in a community with measles cases and one resided in a nearby community with no other cases. The relationship between the cases and their household contacts is illustrated in **Figure 2**. In the diagram, each large black circle represents one household. Seven of the 10 households had direct contact with the index case.

Figure2. Social network diagram of measles cases and household contacts, Alberta, 2013 (N = 67)



The overall household attack rate was 65%, but the non-immunized household attack rate was 100%. In other words, every person in the 10 households who had not received measles-containing vaccine or did not have a self-reported history of disease acquired measles.

Laboratory results

Sixteen of the 42 confirmed cases (38%) were laboratory confirmed. All 16 specimens were sent for genotyping, and 15 were typed. All samples were measles genotype D8 (identical to sequence variant

MVs/Taunton.GBR/27.12), the same sequence variant identified in the ongoing outbreak in the Netherlands (4) and observed in England in 2013 (6).

Public health measures results

Between October 21 and January 3 public health received a total of 7,857 calls regarding measles. This does not include calls made directly to the local MOH or to the measles hotline, whose calls were not consistently tracked. The Mobile Measles Assessment Team was mobilized 84 times during the outbreak, and 167 individuals were assessed in the Measles Assessment Centre. A total of 1,302 individuals were immunized at the eight mass clinics.

Discussion

Imported cases of measles occur in Canada every year, but secondary spread from these cases is usually limited (7). This has generally been the case in Alberta, as this was the first widespread outbreak of measles there since 2000. Because of the direct link of the index case with a large population of susceptible individuals, spread from the index case was expected. However, extensive planning with stakeholders and immediate declaration of an outbreak with confirmation of the index case meant that measles transmission was limited to approximately six weeks. While 42 confirmed cases is still a significant outbreak of measles, it is noteworthy that the cases were contained to 10 households.

There were a few challenges associated with this outbreak. First, public health was aware of a few unreported cases; however, as a result of the strong linkages between public health and the communities, under-reporting of cases was minimal. Second, attack rates for all contacts could not be calculated because of the nature of the public events attended by the index case. Last, given the resources required to manage the outbreak, the data for some public health measures were not consistently tracked, and the data presented are an underestimate.

Despite these challenges, this outbreak of measles was smaller, less severe and shorter in duration than other outbreaks of measles in unimmunized or under-immunized populations seen recently. In 2011, there was a large outbreak of measles in Quebec that lasted almost a year and resulted in 776 cases, with 11% hospitalized and 8% suffering complications (8). Of these, 79% were considered not immune (8). As of February 26, 2014, over 2,600 cases have been reported in the ongoing outbreak in the Netherlands, including 182 hospitalizations and one reported death; 94% of cases were unimmunized (3). Fraser Health declared an outbreak of measles in a group that opposes immunization for religious reasons on March 8, 2014, and, as of April 8, 2014, had seen 375 cases with two hospitalizations (9). These outbreaks in similar unimmunized populations demonstrate how quickly one measles case can turn into a widespread outbreak and emphasize the importance of preparing in advance and taking immediate action.

This outbreak of measles in Alberta highlights the importance of routine childhood immunization, as all cases in the outbreak were unimmunized. Household contacts who reported a history of disease or one dose of measles-containing vaccine did not become infected. There are several barriers to achieving high immunization coverage in a population, including low socioeconomic status (10), difficulty in accessing services (10-12) and lack of knowledge or misinformation about immunizations (11-13). In this population, religious convictions and cultural norms were the main barriers. It is important to identify the barriers specific to a community and work with the community to address these barriers. In this outbreak, building a relationship of trust and respect between local public health and the communities led to a collaborative effort to minimize transmission within the broad community.

After the outbreak, work continues in preparation for a future outbreak of measles. A province-wide comprehensive plan is being compiled and includes a number of measures and activities focused on the following: case assessment, diagnosis, infection prevention and control, public health measures and immunization. In addition, a survey has been conducted among the five health zones in Alberta to determine interactions among non-immunizing communities in the province. The information is currently being analyzed and will be used to help predict where vaccine-preventable diseases might spread within the province.

Conclusion

This measles outbreak highlights the importance of understanding the demographic nature of local communities, of ongoing surveillance of immunization coverage rates, and of collaboration with both internal and external partners. Recognizing that there are many factors that can contribute to the magnitude and severity of an outbreak, the planning prior to the outbreak and the relationship with the community were key components in containing this outbreak to 10 households. To prevent future outbreaks of measles, exploration of strategies for increasing immunization coverage rates in unimmunized populations is critical. When immunization acceptance is not uniform, other public health strategies should be planned and implemented in order to prevent additional spread of measles, e.g. determining interactions among communities to predict spread, as well as establishing relationships with the communities to better implement infection prevention and control measures should an outbreak occur.

References

(1) National Advisory Committee on Immunization. Canadian Immunization Guide: Part 4 - Active Vaccines [Internet]. Ottawa: Public Health Agency of Canada; 2012. http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meas-roug-eng.php

(2) National Center for Immunization and Respiratory Diseases. Measles. Atlanta: Centers for Disease Control and Prevention; 2009. http://www.cdc.gov/measles/about/index.html

(3) National Institute for Public Health and the Environment. Mazelenepidemie 2013-2014. The Netherlands: Ministry of Health, Welfare and Sport; 2014 Feb. http://www.rivm.nl/Onderwerpen/M/Mazelen/Mazelenepidemie_2013_2014

(4) Knol MJ, Urbanus AT, Swart EM, Mollema L, Ruijs WL, van Binnendijk RS, et al. Large ongoing measles outbreak in a religious community in the Netherlands since May 2013. Euro Surveill 2013;18(36).

(5) Alberta Health. Public Health Notifiable Disease Management Guidelines: Measles. Alberta: Government of Alberta; 2013 Nov. http://www.health.alberta.ca/documents/Guidelines-Measles-2013.pdf

(6) Public Health England. Measles cases in England: update to end-June 2013. Health Protection Weekly Report, 2013 Aug 9; 7(32).

(7) Public Health Agency of Canada. Measles. Ottawa, Ontario: Public Health Agency of Canada; 2013 Oct 24. Available from http://www.phac-aspc.gc.ca/im/vpd-mev/measles-rougeole-eng.php

(8) Bureau de surveillance et de vigie. Final report on the provincial outbreak of measles in 2011. Québec: Ministère de la Santé et des Services sociaux; 2012. http://www.msss.gouv.qc.ca/en/sujets/prob_sante/measles/portrait2011.php

(9) Fraser Health. Health Alert: Measles in Fraser East. Surrey, BC: Fraser Health; 2014. http://www.fraserhealth.ca/your_health/immunizations/measles/news-and-updates/

(10) Santoli J, Szilagyi P, Rodewald L. Barriers to immunization and missed opportunities. Pediatr Ann 1998;27(6):366-374.

(11) Mills E, Jadad A, Ross C, Wilson K. Systematic review of qualitative studies exploring parental beliefs and attitudes toward childhood vaccination identifies common barriers to vaccination. J Clin Epidemiol 2005;58:1081-1088.

(12) Lieber M, Colden F, Colon A. Childhood immunizations: A parental education and incentive program. J Pediatr Health Care 2003;17:240-244.

(13) Evers D. Teaching mothers about childhood immunizations. Am J Matern Child Nurs 2001;26(5):253-6.

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Conflict of interest

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A community outbreak of travel-acquired measles, Ontario 2009

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Abstract

Background: Canada has held elimination status for measles since 1998; however, imported cases continue to occur.

Objective: To describe the public health response to an imported measles case in the Waterloo Region of Ontario in May 2009.

Results: Contacts and exposures were traced, and cases were quickly investigated to identify the source. Through routine reporting mechanisms it was found that the index case had likely been exposed while on holiday in Disney World to a laboratory-confirmed measles case in a nine year old unimmunized boy from the United Kingdom (UK). Canada's National Microbiology Laboratory confirmed that the index case had the same D4 measles strain as the UK case and the strain that had been circulating in the UK. In total, one probable case and six confirmed cases were reported. The median age of confirmed cases was 14.5 years (mean age 17 years, range 6 to 39 years). Five confirmed cases (83%) were female. One confirmed case (17%) was hospitalized; no deaths were associated with the outbreak.

Conclusion: This outbreak highlights the importance of collaboration with clinical care, the laboratory and public health at all levels of government to investigate and control a measles outbreak. Global travel and sustained local transmission may continue to pose a challenge with respect to the eradication of measles in developed countries.

Introduction

Measles (rubeola) is an acute viral disease with a case fatality rate of 1-3 per 1,000 cases. Acute encephalitis occurs in approximately 1 of every 1,000 cases. Measles is one of the most highly communicable of all infectious diseases. It is a leading cause of vaccine-preventable deaths in children worldwide, the majority in developing countries (1, 2). Canada has held elimination status for measles since 1998. Nationally, sustained transmission has been eradicated by the current two-dose measles immunization programs and the high vaccine coverage in the general population; however, imported cases continue to occur (3).

On May 25, 2009, a local hospital reported a suspect case of measles in a 10 year old unimmunized female to Region of Waterloo Public Health. The case had presented to hospital, and measles was clinically suspected by an astute pediatrician. The serology result subsequently reported to Region of Waterloo Public Health on May 26, 2009, was positive (measles immunoglobulin M [IgM] reactive). Subsequent testing of urine samples and eye swabs by reverse transcriptase polymerase chain reaction (RT-PCR) detected measles virus ribonucleic acid (RNA), definitively confirming measles. The patient had travelled to Walt Disney World, Florida, from May 3 to 10, 2009.

This paper describes the local public health investigation, including identification of the source of infection, case definition, laboratory investigations, public health actions and risk communications. It highlights the importance of public health and infection control measures along with high community immunization rates to efficiently and effectively prevent further transmission and control outbreaks.

Methods

Source identification

The index case was reported to the Ontario Agency of Health Protection and Promotion and the Ontario Ministry of Health and Long-Term Care in accordance with routine procedures.

Case finding and data collection activities

Cases were defined using the Ontario Ministry of Health and Long-Term Care criteria (**Table 1**) (4).

Table 1. Case definitions: community outbreak of travel-acquired measles, Waterloo Region, May-June 2009

Case classification	Definition
Confirmed	Laboratory confirmation of infection with clinically compatible signs and symptoms in the absence of recent immunization with measles-containing vaccine: • Isolation of measles virus from an appropriate clinical specimen (e.g., nasopharyngeal swab/aspirate/wash and urine); • Detection of measles virus ribonucleic acid (RNA) from an appropriate clinical specimen; • Seroconversion or a significant (e.g., fourfold or greater) rise in measles Immunoglobulin G (IgG) titre by any standard serologic assay between acute and convalescent sera; • Positive serologic test for measles Immunoglobulin M (IgM) antibody using a recommended assay in a person who is either epidemiologically linked to a laboratory-confirmed case or has recently travelled to an area of known measles activity; or • Clinically compatible signs and symptoms in a person with an epidemiologic link (i.e., close contact) to a laboratory-confirmed case.
Probable	• Clinically compatible signs and symptoms in the absence of appropriate laboratory tests and in the absence of an epidemiologic link to a laboratory confirmed case; or • Clinically compatible signs and symptoms in a person with recent travel to an area of known measles activity.
Clinical evidence criteria	Clinically compatible signs and symptoms are characterized by all the following: • Fever greater than or equal to 38.3 degrees Celsius (oral) and • Cough, coryza or conjunctivitis (followed by) • Generalized maculopapular rash for at least three days.

Cases were interviewed by Region of Waterloo Public Health nurses using a measles-specific questionnaire to document their clinical history, immunization history and other risk factors.

Laboratory investigation

Specimens were collected by the attending health care provider for each case. Laboratory testing was done at the Ontario Public Health Laboratory in Toronto, Ontario. Genotyping was conducted at the National Microbiology in Winnipeg, Manitoba.

Public health actions

Region of Waterloo Public Health initiated intense contact tracing for the index case by identifying all activities and exposures within the infectious period.

Regular communication with hospital infection control staff was maintained, and contact management of exposed patients was coordinated. Region of Waterloo Public Health managed community and physician office exposures, and the hospital infection control team managed hospital contacts.

Risk communication

Communication messages for the public and for health care providers were coordinated by Region of Waterloo Public Health and shared in accordance with regular procedures.

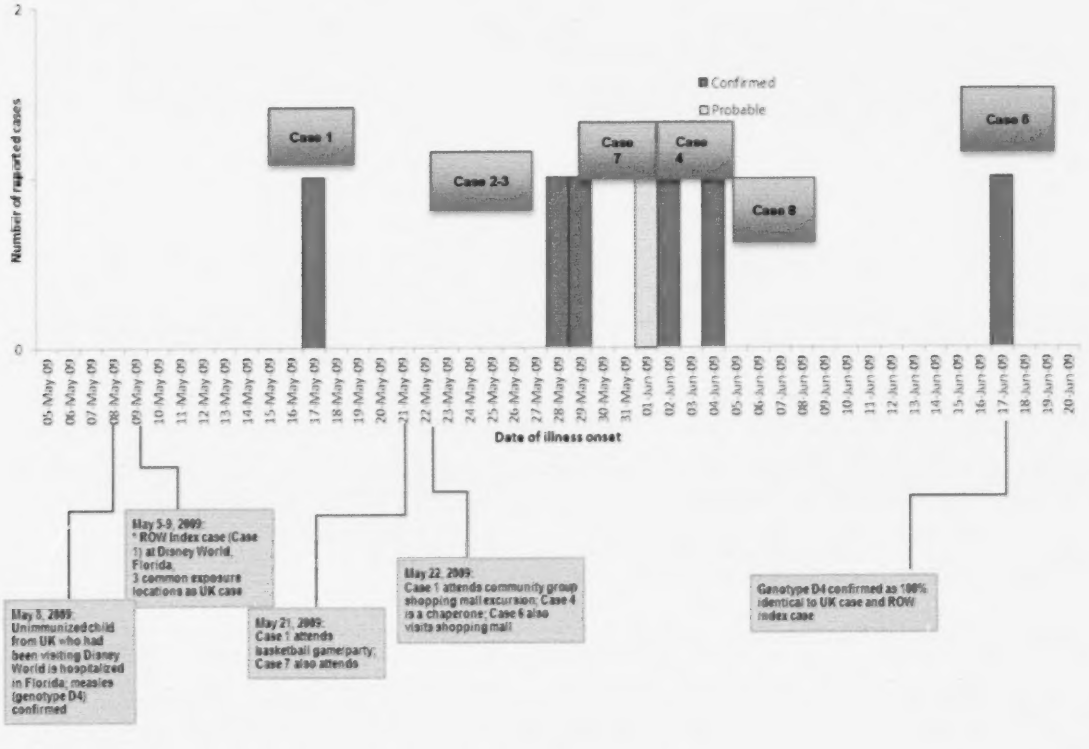
Results

Source identification

The Ontario Ministry of Health and Long-Term Care shared outbreak information with other health units in Ontario and with the Public Health Agency of Canada (the Agency). Given that the index case had spent time in Florida during the exposure period, the Agency contacted the United States Centers for Disease Control and Prevention (CDC).

The CDC subsequently notified the Agency and Region of Waterloo Public Health of a laboratory-confirmed measles case in a nine year old unimmunized male from the United Kingdom (UK) who had visited Walt Disney World from May 1 to 15, 2009. Region of Waterloo Public Health compared the itineraries of the two cases and identified three occasions of possible contact. A timeline illustrating the likely transmission pathway that links the D4 measles strain circulating in the UK to the final measles case in the Waterloo Region outbreak is summarized in **Figure 1**.

Figure 1. Community outbreak of travel-acquired measles, Waterloo Region, May-June 2009


Number of reported cases
Confirmed
Probable
Case 1
Case 2-3
Case 7
Case 4
Case 8
Case 6
Date of illness onset
May 5, 2009: Unimmunized child from UK who had been visiting Disney World is hospitalized in Florida; measles (genotype D4) confirmed
May 5-9, 2009: * ROW index case (Case 1) at Disney World, Florida; 3 common exposure locations as UK case
May 21, 2009: Case 1 attends basketball game/party; Case 7 also attends
May 22, 2009: Case 1 attends community group shopping mall excursion; Case 4 is a chaperone; Case 6 also visits shopping mall
Genotype D4 confirmed as 100% identical to UK case and ROW index case

* ROW=Region of Waterloo

Descriptive epidemiology

In total, one probable case and six confirmed cases were identified (**Figure 1**). The median age of confirmed cases was 14.5 years (mean age 17 years, range 6 to 39 years). Five confirmed cases (83%) were female. One confirmed case (17%) was hospitalized; no deaths were associated with the outbreak. A summary of the reported cases is given below.

Cases 1-3

The index case (Case 1) was an unimmunized 10 year old female who presented to hospital and whose disease was diagnosed by an astute pediatrician. She became quite ill and required hospitalization for several days, but no complications developed. Symptoms included a seven-day prodrome of cough and coryza followed by onset of intermittent fever, a maculopapular rash spreading from face to torso and bilateral conjunctivitis. On day four of the rash onset, measles IgM testing was done, which was reactive. Urine and eye swab RT-PCR testing was done on day 10 of symptom onset, both of which were positive; genotyping of the urine specimen was confirmed as identical to the D4 strain that had been circulating in the south of England since February 2009. A viral culture from the rash done on day 10 of symptom onset was negative. Two unimmunized siblings of the case, aged nine and six years old, showed measles symptoms 14 and 15 days after the index case onset respectively (Cases 2 and 3). These cases experienced a similar but milder course with no conjunctivitis and no requirement for hospitalization. No additional cases of measles were linked to these siblings.

Case 4

Case 4 was a 39 year old female (year of birth 1970) with a three-day prodrome of cough, chills and fever followed by a modified rash described as fine pink spots, which did not become confluent and which faded within two days. Case 4 chaperoned a mall excursion for a community group attended by Case 1 on May 22, 2009. Symptom onset was June 2, 2009, and measles was subsequently confirmed by serology. Immunization records indicated that Case 4 had received measles vaccine at age 11 months and measles mumps rubella vaccine (MMR) at five years of age. Case 4 was a nurse who cared for medically fragile children at a local hospital. She was advised to self-isolate and exclude herself from work; she remained off work until after the fourth day of rash onset. Measles IgM and IgG testing done on day five of rash onset were both reactive. Urine culture and PCR testing done on day eight of symptom onset were negative.

Cases 5-6

On June 24, 2009, a suspect case of measles in a 19 year old male was reported to Region of Waterloo Public Health. He had had no known direct contact with the index case. Case 5 was quite ill and sought medical attention in hospital; he was not admitted but was kept overnight in the emergency room. Symptom onset was June 17, 2009, and included a five-day prodrome of cough, coryza and fever followed by a maculopapular rash and conjunctivitis. Immunization records indicated that he had received two doses of MMR at nine and ten months of age in his country of origin. Measles IgM and IgG testing was done on day two of rash onset. Measles IgM was reactive; measles IgG was non-reactive. Convalescent measles IgG testing done on day 16 of symptom onset was reactive. Nasopharyngeal RT-PCR testing done on day eight of symptom onset was positive, and subsequent genotyping confirmed an identical match to the D4 strain of the index case.

During case management Case 5 indicated that his twin sister (Case 6) had shown similar symptoms on June 4, 2009, 13 days prior to onset of his own symptoms. Case 5 also indicated that his sister spent a lot of time at the local shopping mall associated with the outbreak. Subsequent investigation by Region of Waterloo Public Health determined that Case 6 had indeed been at the local shopping mall associated with the outbreak on May 22, 2009; this was confirmed with a transaction receipt for a purchase made that day. Measles was confirmed in Case 6 by measles IgM and IgG serology testing done one month after rash onset, both of which were reactive. Symptom onset included a five-day prodrome of cough, coryza and fever followed by a maculopapular rash. Immunization records indicated that she too had received two doses of MMR at 9 and 10 months of age in her country of origin. Case 6 was also quite ill and sought medical attention in hospital; she was not admitted but was kept overnight in the emergency room.

RT-PCR and genotyping from Case 5, the final case reported as part of the outbreak, identified the measles strain as D4, 100% identical to the index case in Waterloo (Case 1).

Case 7 (probable case)

Case 7 was an 11 year old female who showed symptoms 11 days after exposure to the index case at the basketball game/party on May 21, 2009. Symptoms were mild and included cough, coryza and sore throat followed by a low grade fever and rash. The rash spread from face to torso but was described as little bumps resolving in two days without becoming confluent. The case had received one dose of MMR vaccine at 13 months of age, at which time the parents decided to discontinue further immunization. Measles IgM and IgG testing was done on day five of the rash onset. The measles IgG was highly reactive, and the IgM was indeterminate. A throat swab for PCR and culture taken on day nine from symptom onset was negative. Further testing was declined by parents. Investigators speculated that this was a modified measles presentation, with minimal viral shedding due to partial immunization. Although this case did not technically meet the Ministry's guidelines [4] for a probable case, it was classified as such, given the strong epidemiological link. An unimmunized sibling of Case 7 did not show symptoms.

Laboratory investigation

Genotyping of the Waterloo index case (Case 1) was confirmed to be a 100% identical match to the D4 strain identified in the UK case and the strain that had been circulating in the south of England since February 2009.

Public health actions

Exposures identified for the index case included hospital and community physician waiting rooms and numerous community activities. Two community activities were of particular interest: a basketball game/party on May 21, 2009, and a community group excursion to a local shopping mall on May 22, 2009.

Active surveillance was initiated by means of direct telephone calls and e-mails to the approximately 87 identified community contacts at risk. One possible susceptible health care worker was identified in the community (Case 4). No susceptible health care workers were identified in the hospital's contact investigation. Immunization was discussed and encouraged with susceptible contacts or their parents; however, many were philosophically opposed to immunization. Susceptible contacts were advised to self-isolate until the end of the potential incubation period, and most were very cooperative. There were no high-risk contacts requiring immune globulin (i.e. immunocompromised people, infants, pregnant women).

Risk communication

Regular written advisories were faxed to all local primary health care providers and hospitals in Waterloo Region to provide case details, recommend increased surveillance, encourage immunization of susceptible individuals, avoid exposure to contacts in waiting rooms and report suspect cases. A media advisory was released to advise the public of the potential exposure date and time frame at the local shopping mall visited by the index case while infectious, and to encourage immunization for those susceptible. Letters and facts sheets were distributed to the families participating in the basketball program.

Discussion

This outbreak illustrates the highly infectious nature of measles and the potential for community-wide transmission from a single case. There was excellent collaboration among local, provincial and federal public health professionals and optimal coordination of public health and clinical care. Infection control practices in hospitals and physician offices likely played a role in preventing transmission. Case 1, Case 5 and Case 6 all spent time in hospital settings while infectious, yet no transmission occurred within the hospital. The high immunization rates in Waterloo Region (traditionally 90%-95% among school-age children from English-speaking publicly funded schools) were also a key factor in preventing further spread.

The six confirmed cases in this outbreak were either unimmunized or inadequately immunized. Case 4 and Case 7 were partially immunized and had milder illnesses and modified transient rashes. In both cases the PCR testing was negative, perhaps as a result of less viral shedding from partial immunization. This could explain the highly reactive measles IgG and no transmission to the unimmunized sibling of Case 7.

Case 5 and Case 6 had immigrated to Canada in 2005 and attended high school for several years in Ontario before moving to Waterloo Region to attend university. They had each received two MMR vaccinations in their country of origin, but at the ages of 9 and 10 months. This illustrates that those moving to Canada from

developing countries may be inadequately immunized and may be a higher priority group. Immigrant populations are not required to demonstrate proof of immunization before entry to Canada and may be a particularly vulnerable group. Cases 5 and 6 were quite ill despite some immunization, perhaps because they had little or no protection. Serology testing for mumps and rubella demonstrated no immunity; both were supportive of immunization and subsequently received two doses of MMR vaccine in accordance with the Ontario immunization schedule.

Transaction purchase receipts are often used in foodborne outbreak investigations in an attempt to verify exposure to an implicated food item. Interestingly, this outbreak demonstrated the usefulness of a purchase receipt to epidemiologically link two previously unrelated cases and establish a connection between all of the reported cases in this outbreak.

Conclusion

This imported case of measles led to a relatively small outbreak of measles in Waterloo Region, given the highly infectious nature of the disease and an urban community of over 500,000 people. Factors that may have contributed to the limited spread within the community include a high rate of immunization, timely outbreak investigation, a high degree of compliance for self-isolation even in families philosophically opposed to immunization, risk communication and collaboration with local health care providers. Global travel may continue to pose a challenge with respect to the eradication of measles in developed countries, which reinforces the importance of maintaining high immunization rates in the community and continued vigilance for sporadic cases with the potential to cause outbreaks.

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References

(1) American Academy of Pediatrics *Red Book 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009.

(2) Mandell G., Douglas R. and Bennett J. *Principles and Practices of Infectious Disease* 6th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2005.

(3) Public Health Agency of Canada. *Canadian Immunization Guide*, 7th ed. Ottawa: Public Health Agency of Canda, 2006.

(4) Ontario Ministry of Health and Long-Term Care. *Infectious Diseases Protocol*, Toronto: Queen`s Printer for Ontario; 2009.

Measles molecular epidemiology: What does it tell us and why is it important?

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Abstract

Background: Measles molecular epidemiology was a key component of the verification of elimination of indigenous measles in Canada and is an invaluable tool during public health investigations, both to establish whether connections exist between concurrent measles cases and to indicate possible sources of importations. There are 24 distinct genotypes however the genotype is usually not sufficient to describe the complex molecular epidemiology of measles cases. The exact genetic sequence of the last 450 nucleotides of the nucleoprotein (N) gene (N-450) is used. The measles genome mutates very slowly and so cases within the same chain of transmission usually have identical N-450 sequences. In Canada, the National Microbiology Laboratory (NML) sequences the N-450 and deposits it into the WHO measles sequence database, MeaNS. This database can be used to identify other geographic regions where the measles sequence was detected, supporting or excluding connections. For commonly detected N-450 sequences, MeaNS designates a "sequence variant." Sequence variants are used as the defining characteristic of measles cases with identical sequences and this designation is fundamental to the description of measles molecular epidemiology both locally and globally. As progress is made towards global measles eradication, its genetic diversity decreases and distinct importations of measles from a single reservoir can be difficult to distinguish using current methods. Extending sequencing methods beyond the N-450 is required. While sequencing the entire hemagglutinin (H) gene, which is currently done routinely at the NML, can be helpful, whole genome sequencing will be required for effective molecular surveillance to monitor the sustained elimination of measles in Canada.insert text here.

Introduction

Canada has eliminated indigenous measles, an achievement documented in a report submitted to the Pan American Health Organization (PAHO)/World Health Organization (WHO) (1). The last endemic measles case in Canada occurred in 1997, and measles was eliminated from the entire region of the Americas in 2002 (2). Measles molecular epidemiology was a key component in verifying the elimination of measles by demonstrating the absence of an endemic genotype and will continue to be critical in the monitoring of measles elimination. Furthermore, measles molecular epidemiology is an invaluable tool during public health investigations, both to establish whether connections exist between concurrent measles cases or outbreaks and to indicate possible sources of importations. This article provides information with which to understand measles genotyping data, to demonstrate both the utility of and need for measles molecular epidemiology in Canada and to provide a discussion of the future directions in an elimination setting.

Measles genotyping 101

An important aspect of disease surveillance is the ability to differentiate lineages, types or variants of a pathogen. This process is generally referred to as typing and, historically, pathogens of the same genus or species would be typed by their phenotypic characteristics, such as biochemical markers (e.g. presence or absence of toxins) or serological markers (the types of antigens present on the pathogen). This is largely the process used for enteric bacteria (*Salmonella, E. coli,* etc.*)* and influenza viruses for example. However, for a number of pathogens, including measles, there are insufficient phenotypic differences to employ this method of typing. The advent of DNA sequencing technology, the process of determining the order and identity of

nucleotides within a DNA molecule, has allowed the identification of distinguishing regions within genomes that can be used for differentiating lineages. This is the process of genotyping.

The WHO has identified 24 phylogenetically distinct measles genotypes, designated A, B1, B2, B3, C1, C2, D1, D2, D3, D4, D5, D6, D7, D8, D9, D10, D11, E, F, G1, G2, G3, H1 and H2, in which the letters identify the main clade and the numbers the subclades (3). Genotypes are groupings of genetically related sequences with inherent variability, and the genotype designation is usually not sufficient to describe the complex molecular epidemiology of measles cases. Therefore the WHO recommends using the exact sequence (or "variant") of the last 450 nucleotides of the nucleoprotein (N) gene (termed the "N-450"), at a minimum, for molecular epidemiology and the entire sequence of the hemagglutinin (H) gene (1854 nt) for additional information (3, 4). Since the measles genome mutates very slowly, usually cases in the same outbreak or chain of transmission carry identical N-450 sequences, and differences, even of one nucleotide, are usually enough to exclude direct transmission between two cases.

The WHO maintains a measles sequence database, MeaNS (5) (http://www.who-measles.org/Public/Web_Front/sequence.php), to which members of the WHO Global Measles Laboratory Network (LabNet) submit sequences (N-450 and H gene) from measles cases. LabNet members are also able to compare the N-450 sequences of their cases to sequences deposited by other members in order to identify other geographic regions where the measles sequence was detected. This information can provide laboratory evidence supporting or excluding connections between imported cases and their countries of export.

For commonly detected N-450 sequences, MeaNS designates a "sequence variant" (3). Examples of sequence variants are MVs/Manchester.GBR/10.09 (genotype D4) and MVs/Taunton.GBR/27.12 (genotype D8). Members of the LabNet interrogate the MeaNS database to determine to which sequence variant the sequence from their measles case is identical. The sequence variant becomes the defining characteristic of measles cases and outbreaks, and is used to easily identify matching measles sequences from other possibly connected cases (within an outbreak for example) or countries of interest.

In Canada, measles genotyping is performed at the National Microbiology Laboratory (NML), a WHO regional measles and rubella reference laboratory. Provincial laboratories are advised to submit all their positive and suspect measles specimens (nasopharyngeal swabs and/or urine) to the NML for genotyping. While all measles cases should be genotyped, only those with adequate specimens can be, and are, genotyped. The NML returns the measles genotyping information, consisting of genotype, "sequence designation" and, where applicable, designation of the identical sequence variant, to the provinces. Sequence designations are the WHO standardized names of measles sequences obtained from individual measles cases. They serve to indicate both the place (city or province, or state and country) and time (by epidemiological week and year of rash onset or specimen collection) of the measles case (3, 4). For example MVs/Ontario.CAN/22.13 is a measles sequence from a case in Ontario, Canada, in the 22nd epidemiological week of 2013. The NML also reports to the WHO by depositing the sequences in MeaNS.

Utility of and need for measles molecular epidemiology

Canada underwent a substantial number of measles cases and outbreaks in 2013, some of which occurred concurrently in different provinces (6). In some cases, identification of the measles genotype alone was sufficient to verify that concurrent outbreaks were indeed distinct (for example, early in 2013 genotype B3 measles cases occurred in Ontario shortly after the separate occurrence of genotype D8 cases in the same province [6]). In contrast, measles genotype D8 was detected throughout the year and in nearly every province that reported measles cases. On the surface this could be alarming for a country that has eliminated measles. Analysis of the sequence data served to demonstrate that the genotype D8 cases could be further characterised as four different sequence variants (6) and thus were not due to widespread circulation of one variant.

In addition to aggregate epidemiological analyses, measles genotyping can provide useful information during real-time investigation of measles cases. In 2013 measles was imported by two Canadian tourists who had independently travelled to the same resort in Mexico [6], another country that has eliminated endemic measles (2). Through genotyping and utilization of MeaNS it was possible to indicate the UK as a possible source of the

virus (Kevin Brown, Public Health, England: personal communication, March 7, 2013), subsequently confirmed by the epidemiological investigation (6).

It should be noted that measles molecular epidemiology relies on the collection and submission of appropriate clinical specimens from all suspected measles cases (nasopharyngeal swab and/or urine; for details see (7) as well as the NML's Guide to Services, available at https://www.nml-lnm.gc.ca/guide2/index-eng.htm). In order to monitor the success of measles elimination programs, the WHO LabNet recommends genotyping at least 80% of all sporadic cases and outbreaks (i.e. genotyping at least one case from ≥ 80% of all outbreaks).

Future directions

The WHO has targeted measles for global eradication (8), and as progress is made the genetic diversity of measles viruses decreases. Often only one measles sequence variant is responsible for large sustained outbreaks, particularly in regions that have not eliminated measles. These outbreaks can be reservoirs for importations of measles into Canada. If there are multiple importations of the same variant, we are unable to distinguish separate importations using current measles genotyping methods. In 2011, the MVs/Manchester.GBR/10.09 sequence variant of genotype D4 was repeatedly imported into Quebec, British Columbia and Ontario and was linked to the large outbreak in Quebec (see [9] and unpublished data). The ability of molecular epidemiology to demonstrate the absence of endemic transmission was challenged. Extending genotyping methods beyond the N-450 to collect additional sequence data for the purposes of finding distinctions between measles cases is therefore required. In 2013, the NML began routinely sequencing the H gene from every measles case. Distinct importations of the D8 strain from the Netherlands (identical to sequence variant MVs/Taunton.GBR/27.12) and unrelated outbreaks and cases of a single measles genotype B3 strain (identical to sequence variant MVi/Harare.ZWE/38.09), both of which were indistinguishable at the N-450, could be differentiated using the H gene sequences (6). However, H gene sequencing is not always sufficient, and as a result whole genome sequencing will likely be required as we move forward toward global elimination.

Conclusion

Measles molecular epidemiology is an invaluable tool for tracking importations, linking cases and demonstrating the absence of sustained measles transmission. As the genetic diversity of measles virus decreases, extended genotyping and eventually whole genome sequencing will be required for effective molecular surveillance. Maintaining high-quality surveillance for measles cases, which includes genotyping (requiring the collection of appropriate specimens) is critical to monitoring the sustained elimination of measles in Canada.

References

(1) Public Health Agency of Canada. Elimination of measles, rubella and congenital rubella syndrome in Canada. Documentation and verification report. December 2011; http://www.phac-aspc.gc.ca/im/vpd-mev/measles-rougeole-mrer-eng.php.

(2) Castillo-Solorzano C C, Matus CR, Flannery B, Marsigli C, Tambini G, Andrus JK. The Americas: paving the road toward global measles eradication. J Infect Dis. 2011; 204(Suppl 1):S270-8.

(3) World Health Organization. Measles virus nomenclature update: 2012. Weekly Epidemiological Record. 2012; 9(87):73-80.

(4) World Health Organization. Standardization of the nomenclature for describing the genetic characteristics of wild-type measles viruses. Weekly Epidemiological Record. 1998; 73:265-272.

(5) Rota PA, Brown K, Mankertz A, Santibanez S, Shulga S, Muller CP, Hübschen JM, Siqueira M, Beirnes J, Ahmed H, Triki H, Al-Busaidy S, Dosseh A, Byabamazima C, Smit S, Akoua-Koffi C, Bwogi J, Bukenya H, Wairagkar N, Ramamurty N, Incomserb P, Pattamadilok S, Jee Y, Lim W, Xu W, Komase K, Takeda M, Tran T, Castillo-Solorzano C, Chenoweth P, Brown D, Mulders MN, Bellini WJ, Featherstone D. Global distribution of measles genotypes and measles molecular epidemiology. J Infect Dis. 2011; 204(Suppl 1), S514.

(6) Public Health Agency of Canada. Measles surveillance in Canada: Trends for 2013; CCDR, 2014; Vol 40-12:195.

(7) Measles and Rubella Elimination Working Group, Health Canada, Public Health Agency of Canada. Guidelines for the prevention and control of measles outbreaks in Canada. CCDR. 2013; 39:ACS-3. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-3/index-eng.php#appa.

(8) World Health Organization. Global eradication of measles: report by the Secretariat. Geneva, Switzerland: World Health Organization; 2010. http://apps.who.int/gb/ebwha/pdf_files/wha63/a63_18-en.pdf.

(9) De Serres G, Markowski F, Toth E, Landry M, Auger D, Mercier M, Bélanger P, Turmel B, Arruda H, Boulianne N, Ward BJ, Skowronski DM. Largest measles epidemic in North America in a decade--Quebec, Canada, 2011: contribution of susceptibility, serendipity, and superspreading events. J Infect Dis. 2013; 207(6):990-8.

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Conflict of Interest

No conflicts of interests to declare.

The challenges of sustaining measles elimination in Canada

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Abstract

Recent importations of measles into Canada have not generally led to large outbreaks, indicating that measles is well controlled in Canada. Isolated large outbreaks that have occurred remind us of the need to remain vigilant. Measles presents particular challenges because it is the most infectious disease known, it thrives among those who do not access the child health system for one reason or another, and we do not always have the information we need to identify and target communities with low immunization coverage. Outbreaks typically arise from Canadians who travel and are exposed to measles abroad. Controlling sporadic outbreaks arising from importations is time and resource intensive, which makes immunization for Canadians travelling outside the region of the Americas (where measles has been eliminated) a priority. To prevent importations of measles into Canada altogether requires other countries and regions of the world to make progress in eliminating measles.

Recent importations of measles into Canada are actually a reminder of the amazing success of immunization in eliminating this disease. This is because, with a few notable exceptions, the majority of importations have either not led to further cases or have caused only small outbreaks, indicating that, overall, measles is currently well controlled in Canada (1). The size of outbreaks (including cases that have no onward transmission) can be used to estimate level of control through calculation of the effective reproduction number (Re), defined as the average number of people actually infected by each case during a specified time period in a population that has some level of immunity (2). Provinces such as Ontario, in which a single case is defined as an outbreak, can calculate Re. Analysis of data from 13 outbreaks in 2009-12 revealed an estimated Re of 0.52, well below the epidemic threshold of Re = 1 (3).

Recent outbreaks of measles in Canada have included typical cases characterized by fever, cough and a maculopapular rash. Patients have been hospitalized, but fortunately there have been no deaths. In 2011, 10 measles deaths occurred in France during a year when epidemics of measles exploded across Europe, with over 30,000 cases reported to the European Centre for Disease Control (4, 5). Following repeated importations from the 2011 epidemic in Europe, Quebec had the largest outbreak of measles of any country in North, Central or South America since 2001, reaching a total of 776 cases between 2011 and 2012. This threatened the elimination status of the whole region (6). The main cause of the outbreak was a level of immunization coverage lower than what was needed for elimination (6), an example of why jurisdictions cannot be complacent and why they need high-quality data on coverage, down to district level and in all age groups, to identify areas at risk and take effective action when gaps in immunity are identified.

We know that gaps in immunity exist in communities that reject immunization or in areas where coverage is just not high enough. Questions that arise about the exact level of immunization coverage and population immunity cannot be answered in the absence of a vaccine registry or sero-surveillance. The fact that three-quarters of cases in 2013 were unimmunized may indicate that coverage is lower than we think, since we would expect most cases to be vaccinated if coverage were high.

Measles presents a particular challenge because it is the most infectious disease known, with a basic reproduction number of around 17 (meaning that in a fully susceptible population, each infected person would, on average, infect 17 others). Population immunity above 95% is therefore needed for elimination (7). Allowing for vaccine failures, this means our system has to reach 97% two-dose coverage to sustain elimination, a

stringent test of the child health system. There is no place to hide from measles, and sooner or later the virus will seek out anyone who is susceptible. This was beautifully demonstrated in the 2013 outbreak of measles in Alberta, in which every person who was exposed and was unimmunized or had no history of measles became infected (8). Outbreaks that have occurred over recent years illustrate how measles immunization coverage needs to be both high and uniform, and how susceptible people cluster together non-randomly. Ascertaining coverage by school and community, as exemplified for southern Alberta, reveals the variation and gaps in immunity and allows public health to develop targeted strategies for improving coverage and plan for outbreaks (9).

Measles shines a light on those who do not access the child health system for one reason or another, including religious groups who reject immunization, children of vaccine-hesitant parents and marginalized groups such as indigenous peoples. Indicators relating to measles immunization programs (coverage, measles mortality) are used as a child health system quality indicator of access to basic public health and primary care, for example as part of the Millennium Development Goals. This approach can be used to compare Canada with other countries, as typified in UNICEF's report on child and maternal well-being, in which Canada ranked at 28 out of 29 countries because of immunization coverage (10). Clearly there is room for improvement. Extremely high quality data are needed at granular levels to be able to demonstrate that we are sustaining control: methods used in the National Immunization Coverage Survey that reach a sample of the population by telephone may be inadequate for this purpose, because responders may not be representative of the general population or be numerous enough to represent smaller communities. Communities that have either not had access to immunization or reject immunization may be small but still large enough to reach the critical community size (250-400,000) required for sustaining measles transmission (11). Religious communities that do not accept immunization may be exposed to measles through their strong links to regions where measles has not been eliminated. We can learn from approaches taken in the Netherlands, where local immunity data were used to explore the impact of vaccination heterogeneity in religious communities linked with those in Canada, and predicted the large outbreak that emerged in the Netherlands in 2013 (12,13).

Rather than being stigmatized as a possible source of risk, immigrants to Canada may actually be important in reducing the risk of measles within this country. While nearly 20% of Canadians were born outside Canada, most came from measles-endemic countries and would have arrived here immune, as a result of having had measles in childhood. As citizens, they are also more likely to be immunized (14). Furthermore, most imported cases have been linked to Canadians who travelled abroad and brought measles back rather than to visitors to Canada (1). This is good news, since Canadians should be easier to reach than visitors, to ensure that they and their children are adequately protected from measles before travel.

Importations are expected as long as measles continues to circulate in other regions of the world. Sustaining measles elimination in the face of such importations is time consuming and expensive, and includes the extensive work of following up cases and contacts and controlling outbreaks. Figures are not available for Canada, but in the United States (US) the cost to public health departments of responding to measles outbreaks in 2011 was US$2.7-5.3 million (15). In this work, a marriage of good public health microbiology and epidemiology is the definition of high-quality measles surveillance and outbreak response. The Public Health Agency of Canada's National Microbiology Laboratory plays an excellent role through genotyping measles cases and is well positioned to deliver the whole genome sequencing that will be needed to provide molecular evidence of the origin of cases (16).

International partnerships, including liaison with the Pan-American Health Organization (PAHO – the regional branch of the World Health Organization [WHO]), are critical to maintaining elimination of measles. In highly decentralized federal countries such as Canada, public health roles are shared among several levels of authority. This can present a barrier to global partners such as PAHO. The Public Health Agency of Canada is responsible for reference laboratory services and reporting weekly to PAHO, but the provinces and territories work with local public health agencies to deliver surveillance and outbreak response. Canada can help in setting an example to the world of how all responsible levels of public health can work together seamlessly and successfully. The US supported the drive to eliminate measles in the region of the Americas in order to reduce the burden of imported measles, and recognizes the value to Americans of controlling measles in other regions (17). Now that measles is being predominantly imported from other regions, it may be time for Canada not only

to sustain elimination within her own borders but also to work with PAHO in our region and WHO globally to support other regions of the world in eliminating measles. In controlling measles, Canada is fulfilling its global obligations. Importations will not cease, however, until measles is eliminated in all the countries of the world. Ultimately this will prevent importations altogether, reduce costs and save lives everywhere.

References

(1) Shane A, Hiebert J, Sherrard L, Deehan H. Measles surveillance in Canada: Trends for 2013. CCDR 2014:40-12,195.

(2) De Serres G, Gay NJ, Farrington CP. Epidemiology of transmissible diseases after elimination. Am J Epidemiol 2000; 151:1039-1048; http://aje.oxfordjournals.org/content/151/11/1039

(3) Lim GH, Deeks SL, Fediurek J, Gubbay J, Crowcroft NS. Documenting the elimination of measles, rubella and congenital rubella syndrome in Ontario: 2009-12. CCDR 2014:40-8.

(4) Number of cases of measles reported to The European Surveillance System (TESSy) by EU and EEA countries, 2011. http://www.ecdc.europa.eu/en/healthtopics/measles/epidemiological_data/Pages/Number-of-measles-cases-2011.aspx

(5) Antona D, Levy-Bruhl D, Baudon C, Freymuth F., Lamy M, Maine C, et al. Measles elimination efforts and 2008-2011 outbreak, France. Emerg Infect Dis. 2013;19(3):357-64

(6) De Serres G, Markowski F, Toth E, Landry M, Auger D, Mercier M, et al. Largest measles epidemic in North America in a decade--Quebec, Canada, 2011: contributions of susceptibility, serendipity, and superseeding events. J Infect Dis. 2013;207(6):990-8

(7) Gay NJ, Hesketh LM, Morgan-Capner P, Miller E. Interpretation of serological surveillance data for measles using mathematical models: implications for vaccine strategy. Epidemiol Infect. 1995;115(1):139-56.

(8) Kershaw T, Suttorp V, Simmonds K, St. Jean T. Outbreak of measles in a non-immunizing population in, Alberta, October-November 2013. CCDR 2014:40-12,219.

(9) Matkin A, Simmonds K, Suttorp V. Measles-containing vaccination rates in Southern Alberta. CCDR 2014:40-12, 212.

(10) Stuck in the middle. Child Well-Being in Rich Countries: A comparative overview. Unicef Canada. Accessed 16th May 2014 http://www.unicef.ca/sites/default/files/imce_uploads/DISCOVER/OUR%20WORK/ADVOCACY/DOMESTIC/POLICY%20ADVOCACY/DOCS/unicef_rc_11_canadian_companion.pdf

(11) Keeling MJ, Grenfell BT. Disease extinction and community size: modeling the persistence of measles. Science. 1997;275(5296):65-7

(12) Glass K, Kappey J, Grenfell BT. The effect of heterogeneity in measles vaccination on population immunity. Epidemiol Infect. 2004;132:675-683

(13) Mollema L, Smits GP, Berbers GA, Van Der Klis FR, Van Binnendijk RS, De Melker HE, Hahné SJ. High risk of a large measles outbreak despite 30 years of measles vaccination in The Netherlands. Epidemiol Infect. 2014 May;142(5):1100-8.

(14) Quach S, Hamid JS, Pereira JA, Heidebrecht CL, Deeks SL, Crowcroft NS, Quan SD, Brien S, Kwong JC; Influenza vaccination coverage across ethnic groups in Canada. Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network Vaccine Coverage Theme Group.CMAJ. 2012 Oct 16;184(15):1673-81. doi: 10.1503/cmaj.111628.

(15) Ortega-Sanchez IR1, Vijayaraghavan M2, Barskey AE2, Wallace GS2Vaccine. 2014 Mar 5;32(11):1311-7. doi: 10.1016/j.vaccine.2013.10.012. Epub 2013 Oct 14. The economic burden of sixteen measles outbreaks on United States public health departments in 2011

(16) Hiebert J, Severini A. Measles molecular epidemiology: What does it tell us and why is it important? CCDR 2014:40-12, 233.

(17) CDC. Manual for the Surveillance of Vaccine-Preventable Diseases. Chapter 7 Measles. http://www.cdc.gov/vaccines/pubs/surv-manual/chpt07-measles.html